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Original Articles

THE CONCENTRATION OF ADRENALINE IN HUMAN PLASMA AND ITS RELATION TO MENTAL ACTIVITY*

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IT is generally accepted that situations of danger, stress or emergency lead to an increased activity of the sympathetic system and to the discharge of adrenaline from the adrenal medulla. Until recently our knowledge was based, essentially, upon two lines of evidence; on the observation of effector organs and mechanisms, such as heart rate, blood pressure, width of skin capillaries, etc., and on the measurement of the adrenaline concentration in the suprarenals or the suprarenal veins, which contain comparatively large quantities. Lately, with the advent of more refined techniques, further methods have become available, which made it possible to estimate adrenaline in tissues other than the suprarenals, in urine and in peripheral blood. The last two methods are obviously of special importance for clinical studies.

In this paper work done in the writer's laboratory will be briefly reviewed. The first part deals with the development of a method for the estimation of adrenaline and noradrenaline in plasma and with experiments that were intended to establish the validity of the method. The concentration of adrenaline and noradrenaline, and the form of their occurrence, in plasma and CSF, will be discussed. In the second part results will be described, which suggest that there is a correlation of the blood-adrenaline level with mental activity.

THE ESTIMATION OF ADRENALINE IN BLOOD

The problem of estimating adrenaline and noradrenaline in blood has attracted many workers (see review by Pekkarinen, 1948), but the methods proposed were lacking in sensitivity or specificity. One of the greatest difficulties was the separation of adrenaline from the plasma proteins. When plasma is treated with any of the common deproteinizing agents, the recovery of added adrenaline in the protein-free filtrate is low, since a large part is adsorbed by the precipitated protein (Gaddum and Schild, 1934; D'Silva, 1937; Lehmann and Michaelis, 1942). Attempts were made to obtain a separation by dialysis or ultra-filtration, but these procedures were not very satisfactory.

* Awarded the Burlingame Prize for 1955.

The problem was elegantly solved by Lund (1949) who showed that adrenaline and noradrenaline were quantitatively retained when plasma, diluted with an equal volume of buffer, was filtered through a column of aluminium oxide at a slightly alkaline pH. The adsorbed amines are subsequently eluted by dilute acid and estimated in the eluate. The column of alumina can be replaced, with equal effect, by one of silica gel (Weil-Malherbe, 1954b).

Since the eluate contains only minute amounts of catechol amines (of the order of 0·01–0·05 μg.) the method of estimation had to be highly sensitive and in this respect a fluorimetric technique seemed most promising. Such a method has been developed by Lund (1949, 1950). Another method, which has been used for the investigations described in this report, is based on a condensation of adrenochrome with ethylenediamine, a reaction which results in the formation of a stable fluorescent compound (Weil-Malherbe and Bone, 1952a, 1953). Compared with the method of Lund it has the advantage of greater simplicity and of requiring less blood; moreover, since the derivative of adrenaline differs in fluorescence from that of noradrenaline, it is possible to estimate both substances side by side in the same solution (Weil-Malherbe and Bone, 1953).

The Validity of the Method

While there is no doubt that the sensitivity of this method is equal or superior to previous methods, it was of the utmost importance to establish its specificity.

To begin with, a large number of individual compounds was tested. Only some closely related amines reacted in a way similar to adrenaline and noradrenaline. Some substances yielded a fluorescent compound on treatment with ethylenediamine, but were not adsorbed on the alumina column; among these were catechol, adrenochrome and 5-hydroxytryptamine. Others, like dihydroxyphenylalanine, formed a fluorescent derivative that was not extracted from the reaction mixture under the conditions used (Weil-Malherbe and Bone, 1952a).

It was next shown that the unknown substance in the plasma behaved like adrenaline in two respects: it had the same rate of disappearance when exposed either to atmospheric oxidation in alkaline solution or to oxidation by a dialysed liver extract. The reactions of adrenaline and of the plasma substance with the liver enzyme were equally inhibited by ephedrine, a specific inhibitor of amine oxidase. Hence it was assumed that the reaction was due to the presence of amine oxidase in the liver extract. When the exposure of plasma to the action of the liver extract was sufficiently prolonged, the reacting material was completely removed (Fig. 1), the time curve being that of a first-order reaction. This indicated that the fluorescence reaction was either given by a single substance or by a mixture of substances with similar affinities for the enzyme.

In a further series of experiments (Weil-Malherbe and Bone, 1953, 1954a) plasma was extracted on a large scale and the purified extracts were studied by paper chromatography. After termination of the run, the paper strip was freed from adherent solvents and cut into sections. Each of these was extracted with dilute acid and the extracts were analysed by the ethylenediamine method. Solutions of authentic adrenaline and noradrenaline were applied to a guide strip; the position of the spots was here revealed with the aid of a spray reagent.

The analysis showed that, after correction for a slight blank, fluorescence was only obtained from those positions that corresponded with the adrenaline and noradrenaline spots on the guide strip. Moreover, the fluorescence obtained

from the adrenaline zone had the same spectral properties as that of the adrenaline derivative, while that given by the noradrenaline zone had the spectral properties of the noradrenaline derivative. The results were essentially the same in two different solvent systems. An example of these experiments is shown in Fig. 2.

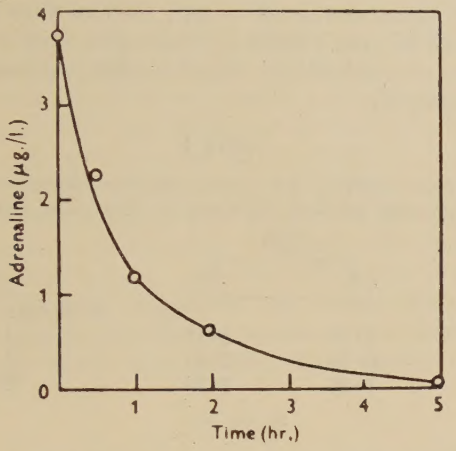

FIG. 1.—Action of amine oxidase on fluorogenic matter in human plasma. From Weil-Malherbe and Bone (1952a).

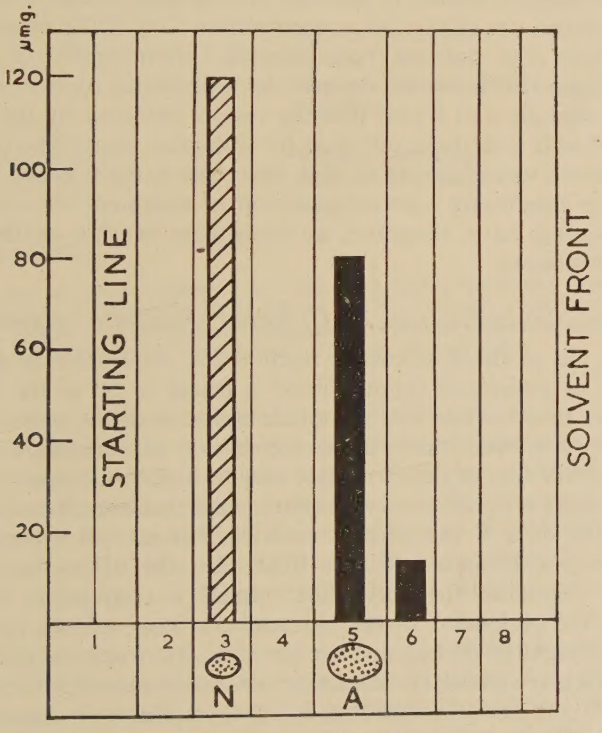

FIG. 2.—Paper chromatography of plasma extract. Solvent: phenol, 75 per cent.—water, 25 per cent. The oblong at the bottom of the Figure represents the paper strip with adrenaline (A) and noradrenaline (N) spots and with approximate position of cuts. The bars indicate quantities of adrenaline (black) and noradrenaline (hatched) calculated from fluorescence of extract of corresponding paper section. Data of Weil-Malherbe and Bone (1954a).

Particular emphasis was laid on the quantitative aspect of these experiments. It was found that the substances isolated by paper chromatography accounted for a proportion of the reacting material of plasma, which closely corresponded with the recovery of added catechol amines in model experiments.

A comparison of the ethylenediamine method with the method of Lund, on portions of the same sample of blood, showed that practically identical results were obtained in both (Table I). This agreement is regarded as highly significant since the two methods are based on different mechanisms, both with a high degree of specificity.

TABLE I

Simultaneous Estimation of Adrenaline and Noradrenaline in Plasma by Ethylenediamine Method (ED) and by Method of Lund (1950)

	ED		Lund	
	A	N	A	N
	(μg./1. of blood)			
1	1·59	5·12	1·56	5·40
2	0·86	2·45	1·15	3·26
3	1·46	3·70	2·37	2·96

A = adrenaline.
N = noradrenaline.

For final identification it will be necessary to demonstrate the biological activity of the catechol amines of plasma. This problem which is a particularly difficult one on account of the low concentrations and of the presence of interfering substances has not yet been studied systematically in the writer's laboratory. Hagen (1954) carried out parallel estimations on fractions prepared from adrenal medulla and found that the results obtained by the fluorimetric method agreed well with those obtained by biological assay. The concentration of catechol amines was of course so high that these extracts could be diluted to the point where interfering substances no longer mattered; the results, though they are reassuring, have, therefore, no immediate bearing on the validity of the method for plasma.

The Concentration of Catechol Amines in Blood

With the aid of the fluorimetric method the concentration of adrenaline in the plasma of peripheral venous blood is found to be of the order of 1–2 μg./1. of whole blood, while that of noradrenaline is of the order of 4–5 μg./1. In the plasma of arterial blood the concentration of adrenaline is about 0·5 μg./1. higher, while that of noradrenaline may be higher or lower than in venous blood. This finding is in harmony with the concept that noradrenaline is secreted not only by the cells of the adrenal medulla, but also at sympathetic nerve endings in peripheral tissues (Euler, 1950). On the other hand, a positive arteriovenous difference for adrenaline implies a continuous utilization of adrenaline by the peripheral tissues. Assuming a basal minute volume of 4 l., a mean body weight of 60 kg., and an identical arteriovenous difference in all parts of the vascular system, an adrenaline utilization rate of 0·033 μg./kg./min. is obtained. A continuous utilization, in turn, implies a continuous discharge of adrenaline. This concept differs from that advocated by Cannon (1929), among others, who maintained that adrenaline is only released in response to stress. According to more modern views, however, adrenaline is discharged continuously from the adrenal medulla, even under basal conditions, provided

the sympathetic innervation is intact. Several authors (Dunér, 1953; Folkow and Euler, 1954; Houssay and Rapela, 1953; Wada and Kanowoka, 1935) have estimated the basal discharge from both suprarenals in cats and dogs and found values of 0·03–0·06 μg./kg./min. These figures are in excellent agreement with the approximate rate of peripheral utilization deduced from the arteriovenous difference of adrenaline. The values for the adrenaline concentration of plasma obtained by the fluorimetric method are therefore compatible with the established adrenaline output of the suprarenals.

Nevertheless, some physiologists assume a much lower level of circulating adrenaline. Holzbauer and Vogt (1954), on the basis of a biological method of assay, came to the conclusion that the resting adrenaline level in the plasma of a normal human subject was below 0·06 μg./l. These authors used a different method of blood collection, designed to prevent the disintegration of the blood platelets. When plasma that had been collected with similar precautions was analysed by the ethylenediamine method it was indeed found that a considerable proportion of the total adrenaline and noradrenaline could be removed by intensive centrifugation, presumably because it was associated with the blood platelets (Weil-Malherbe and Bone, 1954b). Some results are shown in Table II.

TABLE II

Adrenaline and Noradrenaline in Plasma and in Blood Platelets

Exp.	Method of Blood Collection	Fraction	A (μg./l. of blood)	N (μg./l. of blood)
1	NaF-$Na_2S_2O_3$*	Plasma+platelets	1·46	3·70
	Heparin†	Plasma+platelets	1·47	4·25
		Plasma (platelet-poor)	0·34	1·20
		Platelets	0·72	2·11
2	NaF-$Na_2S_2O_3$*	Plasma+platelets	1·06	4·32
	Heparin†	Plasma (platelet-poor)	0·52	2·10
		Platelets	0·53	2·48

A=adrenaline.
N=noradrenaline.

* Three vol. of blood collected in 1 vol. of solution containing 2 per cent. NaF and 3 per cent. $Na_2S_2O_3$ (Weil-Malherbe and Bone, 1952a). Ordinary glassware.

† Blood collected in siliconized glass vessel containing heparin as anticoagulant (200 units/10 ml.). Centrifugations carried out in silicone-coated tubes.

This observation, however, does not completely account for the discrepancy, since even in platelet-free plasma the adrenaline concentration obtained by the fluorimetric method is 5–10 times higher than the upper limit admitted by Holzbauer and Vogt. The writer finds himself in disagreement with Holzbauer and Vogt on another issue: whereas our experiments indicated a reduction of the plasma-adrenaline level during insulin hypoglycaemia by 50 per cent. or more (Weil-Malherbe and Bone, 1952b, 1954c), Holzbauer and Vogt found increases of up to 6 μg./l. in dogs and up to 1·8 μg./l. in a human subject. While it is of course impossible to assert with complete confidence that the fluorimetric method estimates nothing but adrenaline, it is considered highly improbable that it would have failed to detect increases of this order.

The function of the blood platelets as carriers of adrenaline and noradrenaline is in line with the fact that they harbour other pharmacologically active amines, viz. 5-hydroxytryptamine (Rand and Reid, 1951) and histamine, at least in the rabbit (Code, 1952). The results reported in subsequent sections

of this paper were obtained by a method which did not differentiate between free and platelet-bound adrenaline, yet some of the changes observed were so large that they cannot be accounted for by the free fraction alone. It must be assumed therefore that the platelet-bound fraction is a readily available reserve that may undergo extensive changes. This assumption is borne out by preliminary results obtained in experiments on the effect of insulin hypoglycaemia. They show (Fig. 3) that the decrease of concentration elicited by insulin is

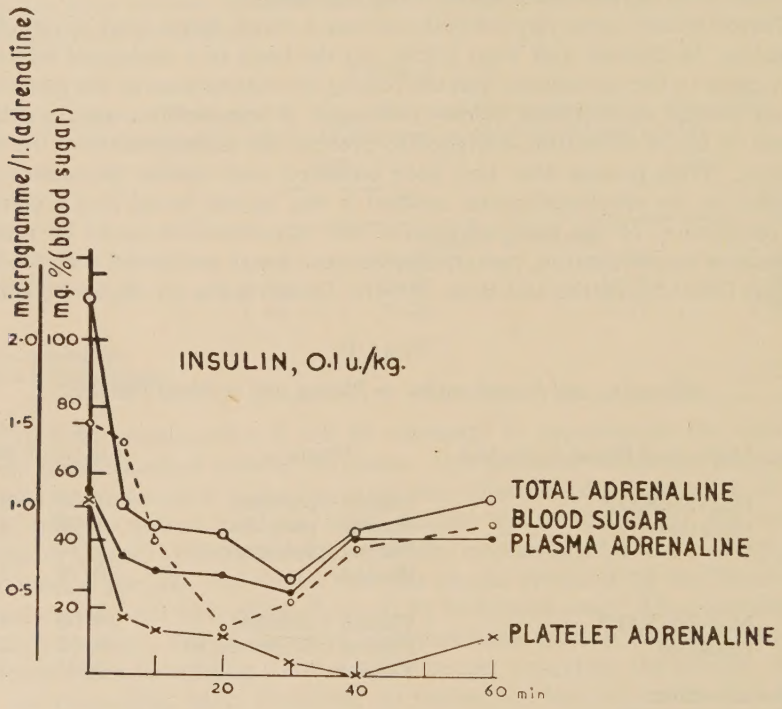

FIG. 3.—Effect of an intravenous injection of insulin (0·1 unit/kg.) on fractions of plasma-adrenaline. (Weil-Malherbe, 1954b.)

relatively much more marked in the platelet-bound, than in the free fraction of plasma adrenaline, and that at one point of the time curve no adrenaline whatever is found to be associated with the platelets. It seems probable, therefore, that, in order to be physiologically active, adrenaline must be released from its association with the platelets.

THE CONCENTRATION OF CATECHOL AMINES IN CEREBROSPINAL FLUID

The fluorimetric method has also been applied to determine adrenaline and noradrenaline in CSF, and mean concentrations of 0·9 μg./l. and 2·5–3 μg./l., respectively, were found (Weil-Malherbe and Liddell, 1954). The levels in CSF were only 40–60 per cent. of the concentration in plasma; the distribution ratio was statistically equal for adrenaline and noradrenaline and hence the ratio of adrenaline/noradrenaline was, on the average, the same in CSF as in plasma.

In some more recent experiments (Table III) the free and platelet-bound fractions of the catechol amines in plasma were determined separately. The corresponding fractions of CSF that had been collected simultaneously were

TABLE III

The Concentration of Adrenaline and Noradrenaline in Plasma and CSF and Their Occurrence in Free Solution and in Association with Particulate Matter

Exp.	Fraction	Concentration (μg./l. of plasma or CSF) A	Concentration (μg./l. of plasma or CSF) N	Ratio CSF × 100 / Plasma (platelet-free) A	Ratio CSF × 100 / Plasma (platelet-free) N
1	Plasma, platelet-poor	1·47	5·05		
	Plasma platelets ..	1·44	5·56		
	CSF, spun at 12,000 *g* ..	0·52	1·58	35·4	31·3
	CSF, precipitate ..	0	0		
2	Plasma, platelet-poor ..	1·00	3·88		
	Plasma platelets ..	1·50	5·35		
	CSF, spun at 12,000 *g* ..	0·52	2·82	52	72·6
	CSF, precipitate ..	(0·10)	(0·35)		

A=adrenaline.
N=noradrenaline.
Blood collected in heparin. Silicone-coated glassware used throughout.

processed by the same methods and with the same precautions as the plasma fractions. Intensive centrifugation had no significant effect on the concentration of the catechol amines in CSF and there is therefore no reason to assume the existence of a fraction of catechol amines associated with corpuscular matter.

A CORRELATION OF THE PLASMA ADRENALINE WITH THE AROUSAL FROM HYPOGLYCAEMIC COMA

The blood level of any substance is the resultant of two opposing processes, the rate of discharge and the rate of disappearance. One has become accustomed to associate a state of increased sympathetic activity with an increased level of blood adrenaline and *vice versa*. On the whole, our findings have shown this view to be justified, although there is one exception: whereas insulin hypoglycaemia is known to stimulate sympathetic activities, it has been found that the intravenous injection of insulin entails an immediate lowering of the plasma adrenaline concentration, which precedes the onset of hypoglycaemia (Weil-Malherbe and Bone, 1954c). The determination of the adrenaline arteriovenous difference revealed that the reduction of the blood level is linked with a transitory increase of the arteriovenous difference, presumably indicating an increased utilization of adrenaline. Further evidence that insulin enhances the utilization of adrenaline is provided by the work of Hökfelt (1951) who found an increased fixation of adrenaline in the liver and heart of insulinized rats, which could be reversed by the administration of glucose. It seems reasonable, therefore, to attribute the depression of the blood-adrenaline level by insulin to an increase of adrenaline utilization in the tissues rather than to a diminished discharge from the adrenal medulla.

It is tempting to connect this phenomenon with the effect of adrenaline on the phosphorylase reaction. Phosphorylase is the enzyme that is responsible for the reversible "phosphorolytic" splitting of glycogen, resulting in the formation of glucose-l-phosphate. The enzyme exists in an active and an inactive form in both liver and muscle. An increase of muscular activity accelerates the conversion of the active form of muscle phosphorylase into the inactive form, presumably because of an increased rate of the phosphorolytic reaction.

Adrenaline has the opposite effect: it accelerates the resynthesis of the active from the inactive form (Sutherland and Cori, 1951; Sutherland, 1951).

Insulin, by pushing increased amounts of glucose into the cell, activates the synthesis of glycogen while the blood sugar is high, particularly in muscle; during the later phases of insulin action, when the blood sugar is low, glycogenolysis is increased, particularly in the liver. Both phases of insulin action therefore lead to an increase of phosphorylase activity. This may be expected to have the same consequence as the increased phosphorylase activity resulting from muscular activity, viz. an increased conversion of the active into the inactive form.

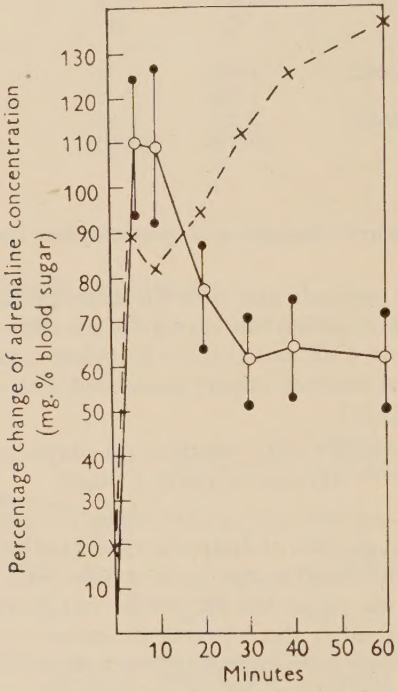

FIG. 4.—The effect of an intravenous injection of glucose (50 ml. 33·3 per cent. solution) on the plasma-adrenaline level during hypoglycaemic coma.
Full line: adrenaline, mean concentration change (per cent.) and its standard error.
Broken line: mean blood-sugar concentration (mg. per cent.).
From Weil-Malherbe and Bone (1954c).

It is suggested that an acceleration of the phosphorylase reaction is the cause of the increased utilization of adrenaline observed after insulin administration.

The spontaneous reversal of insulin hypoglycaemia is preceded by a gradual return of the blood-adrenaline level to its normal value. When, however, hypoglycaemic coma is terminated by the administration of glucose, the blood-adrenaline concentration rises dramatically to a peak well above the normal resting value and subsequently declines to the basal level (Fig. 4). This effect of glucose administration is not confined to insulin hypoglycaemia, but occurs also under the conditions of the simple glucose tolerance test (Fig. 5). The change in the adrenaline concentration is obviously not due to hyperglycaemia, since it precedes the change in the blood-sugar concentration. The effect is specific for glucose, since the ingestion of a fructose meal does not affect the blood-adrenaline level. The blood-noradrenaline level is unaffected by either glucose or fructose ingestion (Weil-Malherbe and Bone, 1954d).

It is difficult to imagine why the administration of glucose would induce an increased discharge of adrenaline from the adrenal medulla, especially in view of the results of Dunér (1953) who showed the existence of a reflex, probably mediated by a hypothalamic centre, by which a rise in blood sugar depresses the secretion of adrenaline by the adrenal medulla. On the other hand, it is likely that the administration of glucose, especially during hypoglycaemia or in the

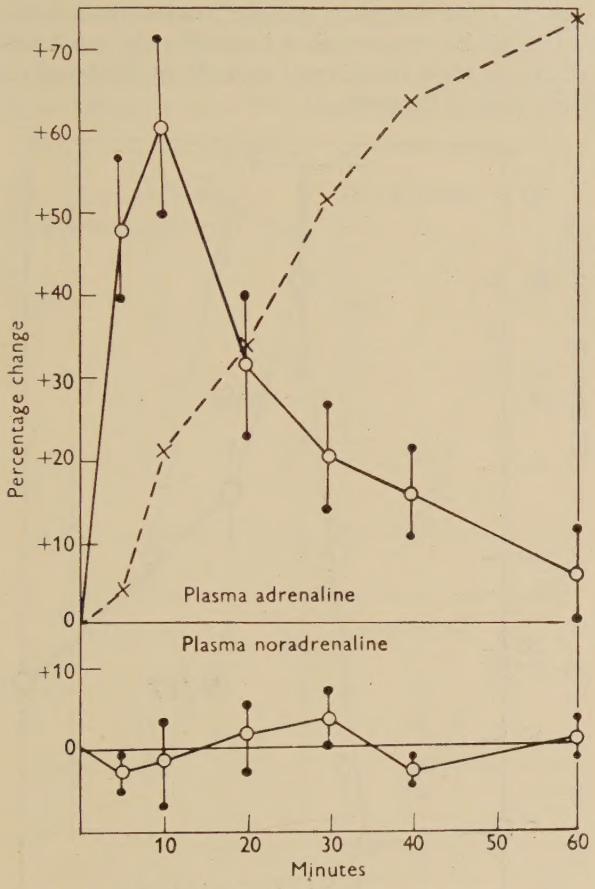

FIG. 5.—The effect of 50 g. glucose, taken by mouth, on the concentration of adrenaline and noradrenaline in plasma.
Broken line: mean concentration change of blood sugar.
From Weil-Malherbe and Bone (1954d).

post-absorptive state, reduces the activity of phosphorylase—and thereby the utilization of adrenaline—because exogenous glucose replaces the glucose mobilized from the glycogen reserves of the body. This mechanism is the logical counterpart of that proposed to explain the effect of insulin on the blood-adrenaline concentration.

When glucose is given intravenously during hypoglycaemic coma, consciousness usually returns within 5 minutes of the injection, coinciding with the peak of the blood-adrenaline curve. After the administration of glucose by nasal intubation arousal may be delayed for 10–30 minutes or more. It was observed regularly in a series of experiments that the time of arousal closely

corresponded with the peak of the blood-adrenaline curve. The simultaneity of these events suggested a causal relationship.

If we assume that adrenaline has other functions in addition to that concerning phosphorylase, then a decrease of adrenaline utilization in the phosphorylase reaction may, by raising the adrenaline concentration in blood, cause their stimulation. If the arousal from hypoglycaemic coma is connected with those other functions of adrenaline, it should be possible to obtain the same result that is observed after glucose administration by other means capable of elevating the blood-adrenaline concentration, such as the stimulation of adrenaline discharge from the adrenal medulla or the injection of exogenous adrenaline. This is indeed the case.

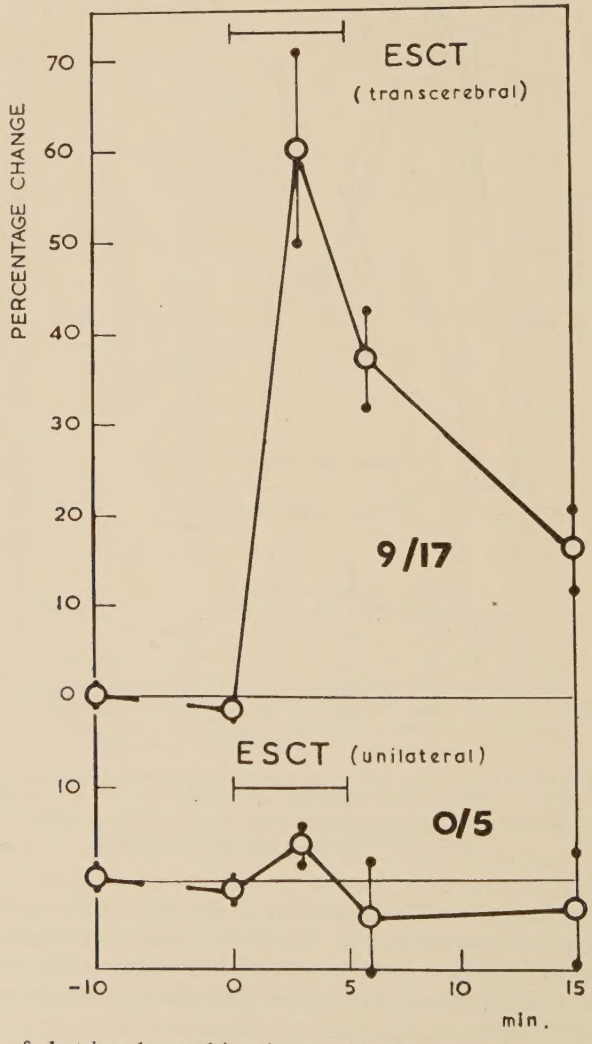

FIG. 6.—Effect of electric subconvulsive therapy (ESCT) on the concentration of catechol amines in plasma during hypoglycaemic coma.
The points indicate mean concentration changes and their standard errors.
The barred horizontal line indicates the duration of ESCT.
Top curve: electrodes in standard biparietal position.
Bottom curve: electrodes on one side of skull.
The ratios show the proportion of cases roused. Data of Weil-Malherbe and Bone (1952b).

Fig. 6 shows the mean percentage change of the concentration of catechol amines in blood resulting from the application of a subconvulsive electric current during hypoglycaemic coma.* The first two blood samples were taken before the treatment, with a 10-minute interval; their agreement shows the absence of spontaneous change during this period. The next blood sample was collected 3 minutes after switching on; it showed an increase of about 60 per cent. Treatment was discontinued after 5 minutes. One minute later the catechol amine concentration was only 37 per cent., and 10 minutes later 16 per cent., above the initial value. In spite of the fact that the elevation of the catechol amine level was poorly sustained, arousal was achieved in 9 cases out of 17 (Weil-Malherbe and Bone, 1952b). No effect either on the catechol amine level

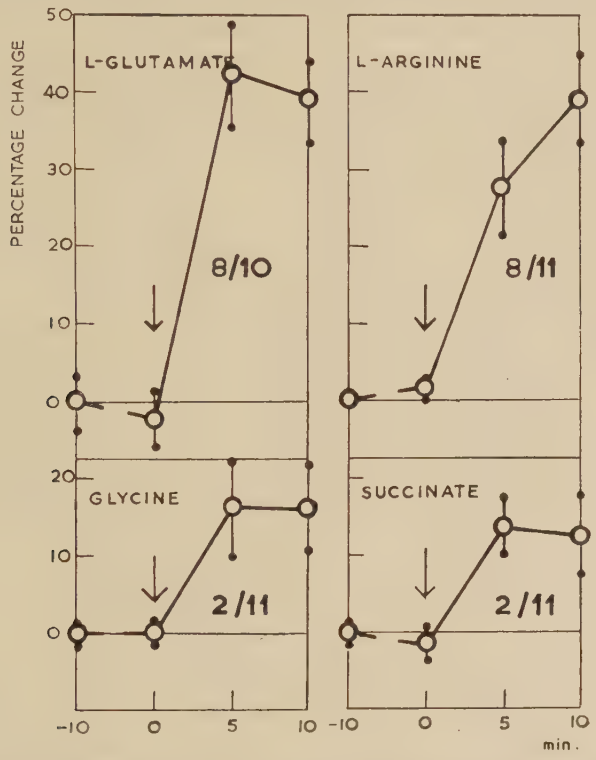

FIG. 7.—Effect of intravenous injection of various substances on the concentration of catechol amines in plasma during hypoglycaemic coma. The points indicate mean percentage concentration changes and their standard errors. The arrow indicates the moment of injection. The ratios show the proportion of cases roused. Data of Weil-Malherbe and Bone (1952b).

in blood or on the comatose state was observed when both electrodes were placed on the same side of the skull instead of in the usual biparietal position. The subjects chosen for these experiments had previously given a positive response to the same current when the standard electrode position was used. It may be concluded that the effect is only observed when the current is conducted across the brain and that it is presumably due to a stimulation of autonomic centres.

An increase of the catechol amine level in blood was also observed when certain amino acids were injected intravenously during hypoglycaemic coma. Fig. 7 shows the mean percentage changes produced by 3 amino acids, L-

* These experiments were carried out in collaboration with Dr. J. D. Montagu.

glutamic acid, L-arginine and glycine, and by a related dicarboxylic acid, succinic acid. All substances were injected in amounts of 0·017 moles dissolved in 10 ml. and adjusted to pH 7·0. The first 2 blood samples, withdrawn before the injection, show the absence of spontaneous change within a period of 10 minutes. The ratios shown in Fig. 7 refer to the proportion of cases in whom consciousness was restored by the treatment. With glutamic acid and arginine 8 successes were achieved out of a total number of 10 or 11 experiments, respectively. With glycine and succinic acid, however, only 2 successes were scored out of 11 tries in each case. Correspondingly, the catechol amine level was markedly raised by the first 2 substances, much less by the second two. There is thus a clear-cut correlation between the effects on consciousness and on the blood-adrenaline level (Weil-Malherbe and Bone, 1952b).

Finally, arousal from hypoglycaemic coma is observed in a high proportion of cases (9/11) when adrenaline itself is administered by slow intravenous infusion (Weil-Malherbe, 1949).

It is concluded from these results that the coincidence of arousal with the rise of the plasma-adrenaline concentration is due not to a merely chronological, but to a causal relationship.

The Plasma-Adrenaline Level During Anaesthesia and Convulsive Activity

Further evidence for a connection between the blood-adrenaline level and the activity of the nervous system was obtained in studies dealing with the effects of various forms of electroconvulsive therapy (E.C.T.). In these experiments (Weil-Malherbe, 1955) electrical convulsions were produced (1) without modification, (2) after barbiturate administration and (3) after the combined injection of a barbiturate and a paralysing agent. The effect of leptazol convulsions, with and without modification by a paralysant, was also investigated. Four blood samples were collected during each treatment, 2 before and 2 after the seizure. In the experiments in which unmodified E.C.T. was used, and also in those in which leptazol, with or without modification, was used, the second sample was withdrawn 10 minutes after the first, but before the treatment was started; it thus served merely to show the absence of spontaneous variation (Figs. 8 and 9). In the experiments in which modified E.C.T. was studied the second blood sample was withdrawn within 1 minute after the injection, but before the application of the current. The injection of the barbiturate was followed by an immediate and dramatic reduction of the plasma-adrenaline level, which was unchanged by the addition of a paralysant (Brevedil M, succinylcholine). In the third blood sample which was collected as soon after the fit as twitchings or convulsions had ceased, a striking increase of the blood-adrenaline concentration was found. Ten minutes later, when the fourth blood sample was taken, the adrenaline level had returned to about the initial value; in those experiments in which a barbiturate was given it returned to a value below the initial level, indicating the persistence of some sedative action. But the rise of the adrenaline concentration in response to the convulsion was only slightly reduced when a barbiturate was injected. Measured by the difference of the adrenaline levels found in samples 3 and 4, the extent of the response is about equal in the 3 forms of E.C.T. After leptazol convulsions the rise of the adrenaline concentration is almost twice as great as after E.C.T. and this effect, too, is not significantly changed by the administration of a paralysant (Brevedil E).

The noradrenaline concentration of plasma is raised by about 40 per cent. after an unmodified convulsion, whether produced by electricity or leptazol. The effect decays more slowly than the adrenaline response and the level is still significantly elevated after 10 minutes. However, the noradrenaline response is completely suppressed when the convulsion is modified by a paralysant, and almost completely, when it is modified by a barbiturate. The rise of the noradrenaline concentration in plasma is thus clearly the result of secondary sequelae of the unmodified procedures, such as muscular contractions, cardiovascular changes and anoxia. The adrenaline response, on the other hand,

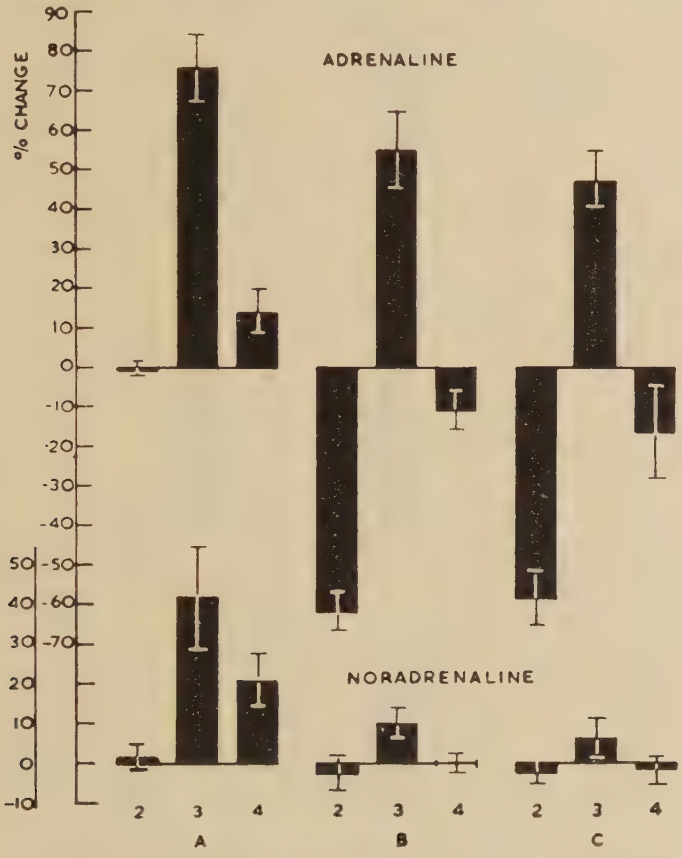

FIG. 8.—The effect of various forms of electroshock on the concentration of adrenaline and noradrenaline in plasma.

The bars indicate the mean percentage concentration changes in samples 2, 3 and 4 of each series. The barred lines indicate the standard error. A=unmodified E.C.T.; B=E.C.T. after injection of hexobarbitone; C=E.C.T. after combined injection of hexobarbitone and Brevedil M. From Weil-Malherbe (1955).

seems to be more directly connected with the increased neuronal activity of the convulsive discharge.

The inhibition of neuronal activity in anaesthesia has the opposite effect on the plasma-adrenaline level. The barbiturate used in these experiments was hexobarbitone, but other barbiturates act similarly, e.g. pentothal (Montagu, 1955) or sodium amytal.

What is particularly remarkable, is the rapidity with which the adrenaline level in plasma may change; thus, the change from the resting level to a value

60 per cent. below the resting level, and from there to a value 60 per cent. above the resting level is observed within the space of about 3 minutes, consequent upon the barbiturate injection and the electric shock, respectively.

Only a very superficial degree of anaesthesia was produced by the dose of hexobarbitone chosen. An effect on the plasma-adrenaline level is even found with purely sedative doses, such as are used as adjuvants to psychotherapy.

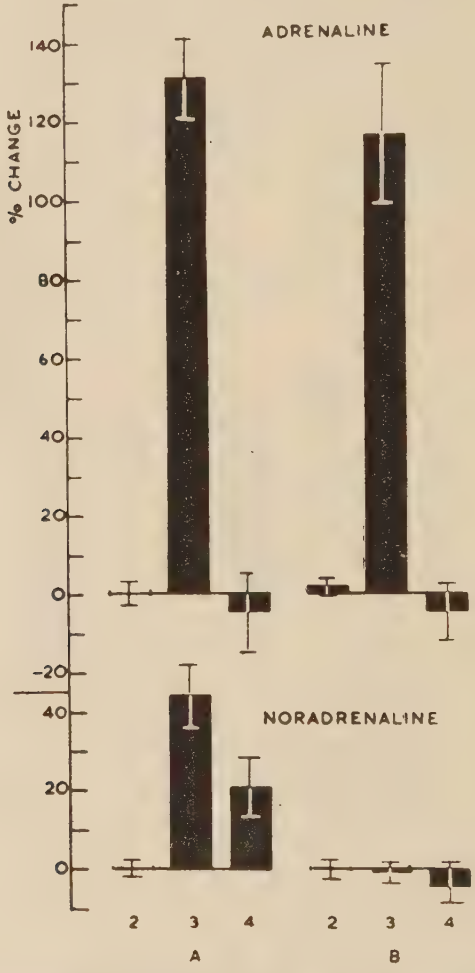

FIG. 9.—The effect of leptazol shock, with (B) and without (A) Brevedil E, on the concentration of adrenaline and noradrenaline in plasma. The bars indicate the mean percentage concentration changes, with the standard error shown on top. From Weil-Malherbe (1955).

The following case report may be of interest:

A woman of 35 was severely affected by ideas of depersonalization from which she experienced relief only under sodium amytal sedation. After a course of sodium amytal treatments it was suggested to her, under hypnosis, that she would receive her usual injection and that she would experience, post-hypnotically, her usual relief. After the suggestion had been made, the previously anxious and agitated patient manifested the symptoms of relaxation, sedation and somnolence and felt relief from her obsession, as she did previously after

sodium amytal injection. The change of the blood-adrenaline level was studied during a real and a suggested sodium amytal treatment and the results are shown in Table IV. It is evident that the suggestion had only a very slight effect on the blood-adrenaline level compared with the effect of the actual injection. Incidentally, this analysis was carried out before the method of differential estimation of adrenaline and noradrenaline was developed. The results are given in terms of catechol amines and the changes would probably have been more marked if it had been possible to estimate adrenaline separately.

TABLE IV

The Effect of an Actual and a Suggested Injection of Sodium Amytal (0·25 g., i.v.) on the Catechol Amines of Plasma. See Text

Exp. 1: Injection		Exp. 2: Hypnosis	
Time (minutes)	Catechol Amines (μg./l. of plasma)		Catechol Amines (μg./l. of plasma)
0	3·43	Before hypnosis	3·56
10	2·68	Under hypnosis	3·51
30	2·50	5 minutes after suggested "injection"	3·44
60	2·74	Half-hour post-hypnotic	3·39
90	2·92		
120	3·37		
240	3·46		

It is to be expected that the spontaneous seizures of epilepsy affect the blood-adrenaline level in the same way as seizures induced by electricity or leptazol. Unfortunately, it has not yet been possible to study a spontaneous epileptic fit, but observations were made on a patient whose EEG showed evidence of epileptic discharge in response to photic stimulation (Fig. 10). Two experiments are illustrated in Fig. 11. The height of the blacked-in columns indicates the plasma-adrenaline level, while the plasma-noradrenaline level is shown by the overall height of the column, including the black part. In the first experiment (Fig. 11, A) photic stimulation was carried out intermittently for 1–2 minutes, followed by several minutes' rest. Each stimulation produced an increase of the adrenaline concentration that was not very large, but probably significant, since the same resting level was reached in the intervals. There was a drop of the noradrenaline level during the experiment, but this could not in any way be related to the procedure. In the second experiment (Fig. 11, B) stimulation by a frequency that did not evoke an EEG response had no effect on the plasma-adrenaline level, but a considerable increase was found in three successive samples withdrawn immediately after periods of stimulation by the critical frequency. The noradrenaline level again showed a tendency towards a decrease without a clear correlation with the experimental procedure. The EEG response to photic stimulation and at the same time the effect on the plasma-adrenaline level was completely suppressed in this case by barbiturate medication.

The Plasma Adrenaline Level During Natural Sleep

It may be argued that the reduction of the plasma-adrenaline level by anaesthetics is not connected with their action on the CNS, but due to a peripheral mechanism. The effect of natural sleep on the adrenaline concentration in plasma has therefore been investigated (Renton and Weil-Malherbe, 1955).

In these experiments a sphygmomanometer cuff was tied around the subject's arm above the elbow when he went to bed. The cuff was inflated while he was asleep, and though this usually woke him up, the arterial circulation of the forearm was arrested and a venous blood sample was taken immediately.

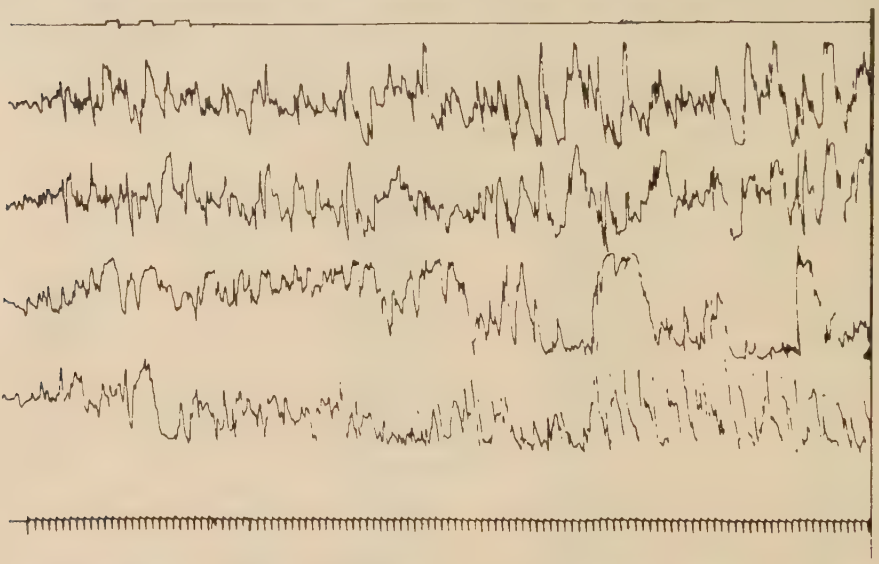

FIG. 10.—EEG response to photic stimulation. The bottom tracing is a photoelectric record of the stroboscope pulses.

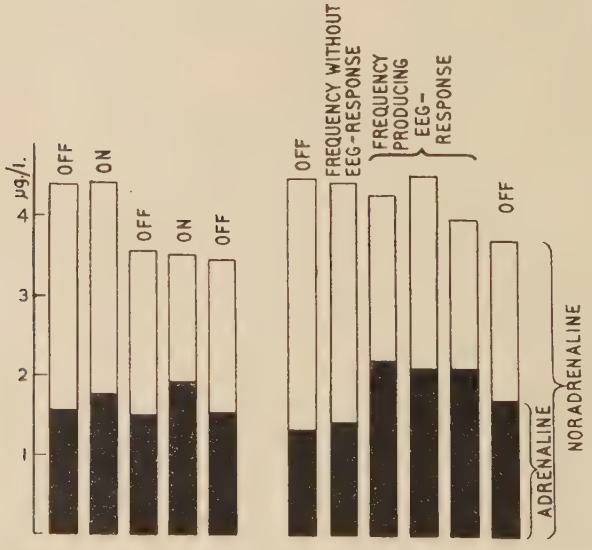

FIG. 11.—Effect of photic stimulation on the concentration of adrenaline and noradrenaline in plasma. Cf. text. (Weil-Malherbe, 1954b.)

Further blood samples were taken either 5–10 minutes after waking or on the following morning before breakfast, or at both these times. Table V shows the mean percentage increase of the plasma adrenaline level of the "waking" samples compared with the "sleeping" sample. The increases are significant

TABLE V

The Effect of Natural Sleep. Mean Percentage Concentration Changes of Adrenaline and Noradrenaline in Plasma after Waking, Compared with "Sleeping" Sample

	No. of Observations	Adrenaline	Noradrenaline
5–10 minutes after waking	10	+37·75%	+7·6%
Standard Error		6·19	4·88
P		<0·01	~0·15
Next morning (fasting)	13	+26·06%	−2·9%
Standard Error		7·08	3·06
P		<0·01	~0·35

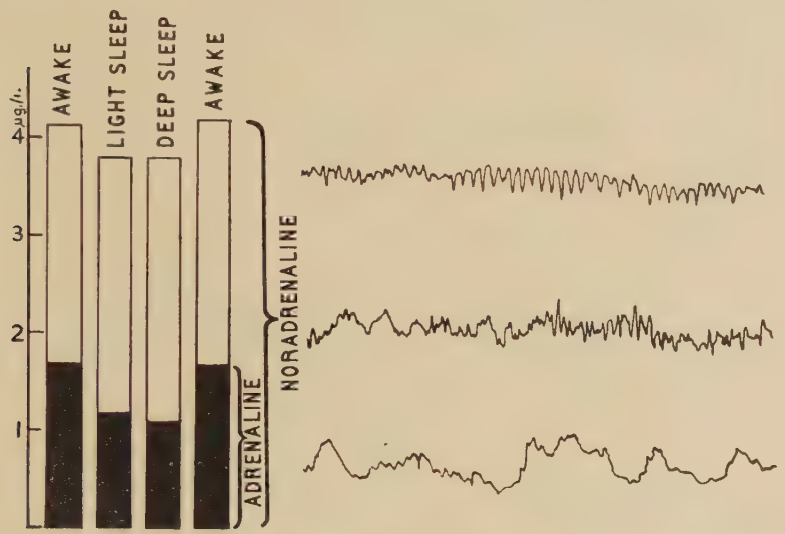

FIG. 12.—Concentration changes of adrenaline and noradrenaline in plasma during sleep. Cf. text. (Renton and Weil-Malherbe, 1955.)

whether the sample was collected immediately on waking or on the following morning. There was no significant effect on the plasma-noradrenaline level.

Another experiment, illustrated in Fig. 12, was performed on a healthy volunteer who stayed up all night and, on the following day, went to sleep while his EEG was recorded. Blood samples were taken before he went to sleep (normal alpha rhythm, top tracing of Fig. 12), when his EEG record indicated light sleep (middle tracing of Fig. 12), again when the record indicated deep sleep (bottom tracing of Fig. 12) and finally when he was awake at the end of the experiment. The plasma-adrenaline level, represented by the black columns, dropped during sleep and returned to the initial value after waking. There was also a slight reduction of the noradrenaline level during sleep.

The effect of sleep, though significant, is smaller than that of anaesthesia, which is not surprising in view of the ease with which natural sleep is reversible.

The Effect of Some Relaxant Drugs on the Plasma-Adrenaline Level

Not all reductions of the plasma-adrenaline level are of central origin. Preliminary experiments have shown that adrenergic or ganglionic blocking agents, such as dibenamine or hexamethonium, have this effect. In particular,

two drugs have been studied, which are now widely used in psychiatry for their relaxing and sedative effects: myanesin (Fig. 13) and largactil (Fig. 14). Myanesin, in doses of 2 g. by mouth, led to a fall of the adrenaline level in the 5 cases investigated. The effect was at its maximum after about $\frac{1}{2}$ hour when the mean concentration was reduced by 50 per cent., a change that was statistically significant. There was also a tendency for the noradrenaline concentration to decrease, but this effect was less consistent. Largactil was injected intramuscularly in doses of 100 mg. In the 3 cases investigated, so far, a reduction of the adrenaline level was observed in two. The third case showed an initial rise, followed by a drop. Similar biphasic reaction curves were previously observed after the injection of methedrine and lysergic acid diethylamide (Liddell and Weil-Malherbe, 1953). The changes of the noradrenaline level observed after largactil medication again showed no definite trend or pattern and are difficult to interpret.

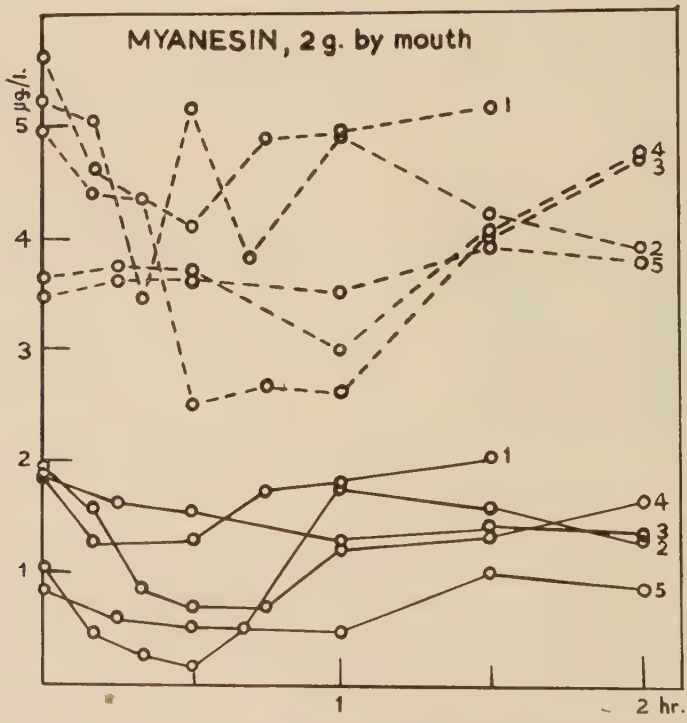

FIG. 13.—Effect of myanesin on the concentration of adrenaline (full lines) and noradrenaline (broken lines) in plasma. (Weil-Malherbe, 1954b.)

Clinically these drugs were found to alleviate symptoms of tension, anxiety and agitation, subjectively and objectively. Their mechanism of action is not yet fully understood and the writer does not wish to imply that they are peripheral blocking agents, but whatever the mechanism, it is relevant that a decrease of mental and physical tension is associated with a decrease of the plasma-adrenaline level.

THE PLASMA-ADRENALINE LEVEL IN MENTAL DEFICIENCY AND SENILE DEMENTIA

Although the investigations described in this section arose from an entirely different hypothesis, they turned out, in the end, to have some bearing on the

relationship between mental activity and the blood-adrenaline level. The original hypothesis was that the metabolic error of phenylpyruvic oligophrenia might entail an impairment of adrenaline synthesis; since the formation of tyrosine from phenylalanine is blocked in this condition and since tyrosine is the precursor of adrenaline, such a possibility was worth considering. When it was found that the plasma-adrenaline level was indeed abnormally low in these cases, the study was extended to other forms of congenital mental deficiency and to a group of patients suffering from senile dementia. For comparison, the results of adrenaline estimations obtained during one year in various groups of patients were collected (Weil-Malherbe, 1954a).

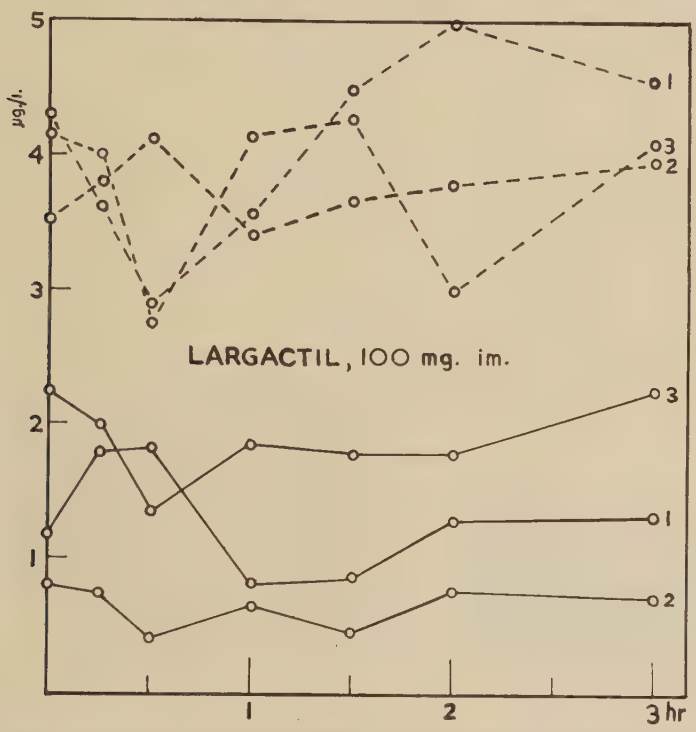

FIG. 14.—Effect of largactil on the concentration of adrenaline (full lines) and noradrenaline (broken lines) in plasma. (Weil-Malherbe, 1954b.)

In Fig. 15 the results are shown in the form of a histogram, with the bars arranged in the order of increasing adrenaline concentration. Each bar represents the mean value of the plasma-adrenaline concentration, with the limits of the standard error indicated by the barred line. The figures at the foot of each column indicate the number of observations and the number of cases. The two figures do not always tally, because some cases were examined repeatedly. Wherever multiple observations from the same individual were available, the mean value was calculated and entered as a single observation when the group average was computed. On the whole, the individual variation was similar to the variation within the group. Only blood samples that were collected under basal conditions were used for this survey.

On the left of Fig. 15 are 5 oligophrenic groups, on the right are groups of mental hospital patients and, in addition, a group of peptic ulcer patients, most of whom have had a gastrectomy; their blood samples were sent to us from

another hospital. These groups are very heterogeneous, including, as they do, cases of psychosis, both acute and chronic, psychopathy and neurosis, as well as organic diseases. What they had in common was the fact that their intellectual faculties were not grossly impaired.

Congenital mental defectives other than those belonging to the group of phenylpyruvic oligophrenia were classified as idiots, imbeciles and feeble-minded persons by conventional criteria. The group of idiots contained one case of hemiplegia and one of mongolism. Among the imbeciles were 8 cases of epilepsy, 2 of mongolism, 2 of spastic diplegia and 1 of microcephaly. The remainder of these groups was free from somatic abnormalities. Of the 13 cases of phenylpyruvic oligophrenia 7 were classified as idiots and 3 as imbeciles. No information was available on the remaining 3 cases.

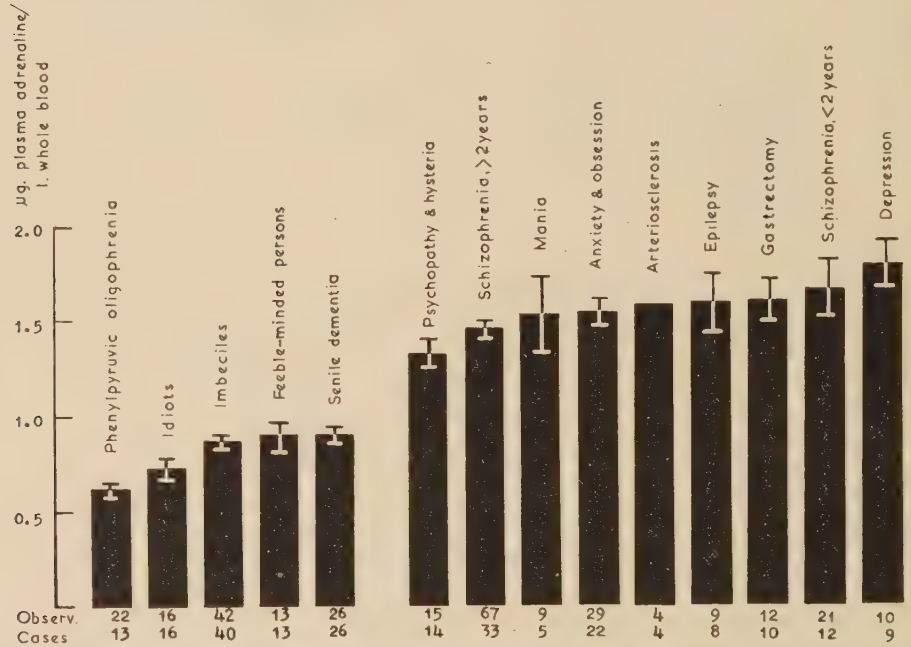

FIG. 15.—Mean plasma-adrenaline concentration in various groups of oligophrenic and non-oligophrenic patients. The barred lines indicate the standard error of the mean. (Data of Weil-Malherbe, 1954a.)

If the oligophrenic groups are considered first, it appears that the average plasma-adrenaline level is lowest in the group of phenylpyruvic oligophrenia, a little higher in the group of idiots, and higher still in the remaining three groups, which have almost identical mean values. This order suggests a correlation with the severity of the mental defect. The difference between the group average of the phenylpyruvic oligophrenia cases and the common mean of the other mental deficiency groups is statistically significant.

As far as the non-oligophrenic groups are concerned, it is remarkable how slight are the variations among the average plasma-adrenaline levels of the different sub-groups, in spite of their heterogeneity. The psychopathy-hysteria group deviates most from the common average in the negative direction, the depression group most in the positive direction. The difference between these two groups is significant, while those between most of the other groups are not (cf. Weil-Malherbe, 1954a).

Compared with the differences among the sub-groups, the difference between the oligophrenic groups on the one hand, and the non-oligophrenic groups on the other is quite striking. The common average of the latter exceeds that of the former by 83 per cent., a difference that is highly significant (Table VI).

TABLE VI

The Concentration of Adrenaline and Noradrenaline in the Plasma of Oligophrenic and Non-oligophrenic Hospital Patients

Groups	No. of Cases	Adrenaline			Noradrenaline		
		Mean (μg./1. of blood)	S.E.*	P†	Mean (μg./1. of blood)	S.E.*	P†
Non-oligophrenic, combined	117	1·52	0·035		4·10	0·062	
Oligophrenic, combined ..	108	0·83	0·024	<0·01	3·79	0·069	<0·01
Oligophrenic, omitting phenylpyruvic oligophrenia	95	0·86	0·025	<0·01	3·84	0·071	<0·01
Oligophrenic, omitting senile dementia and phenylpyruvic oligophrenia ..	69	0·84	0·030	<0·01	3·83	0·090	0·015

* S.E.=Standard Error of Mean.

† P=probability that difference from mean of combined non-oligophrenic groups is due to chance.

The groups are fairly well matched with regard to sex, but not so well with regard to age. The 3 mental deficiency groups (idiots, imbeciles and feeble-minded persons) consist of adults up to the age of 57 and are closest in age distribution to the bulk of the non-oligophrenic groups. The phenylpyruvic oligophrenia group contains only children up to the age of 13, while the group of senile dementia patients is composed of people in their seventies and over. Among the non-oligophrenic groups is a small group of 4 patients, aged 64–78, who suffered from arteriosclerosis without intellectual deterioration. The group was too small to calculate its standard error, but the agreement with the mean values of the other non-oligophrenic groups is sufficiently close to attribute the low values found in the senile dementia group to causes other than old age. We have also had an opportunity of analysing some blood samples of normal children; in most of them values were found that were normal by adult standards. The possibility must further be conceded that, in the case of phenylpyruvic oligophrenia, the depression of the plasma-adrenaline level is a consequence of the metabolic error rather than the mental defect. But even if the group of phenylpyruvic oligophrenia is omitted, the general conclusions remain unchanged (Table VI).

Fig. 16 shows the mean values of the plasma-noradrenaline levels in the same groups, arranged in the same order as in Fig. 15. The differences are smaller than those of the plasma-adrenaline levels. The average noradrenaline level of the oligophrenic groups is only about 7 per cent. below that of the non-oligophrenic groups, but, small though this difference is, it is statistically significant. The result remains the same even if the phenylpyruvic oligophrenia group —where the noradrenaline level is most strongly depressed—is omitted (Table VI).

These observations show that dementia and mental deficiency of different aetiology are associated with a reduced level of circulating adrenaline. It is tentatively suggested that this effect is a symptom of the reduced mentation processes in these patients.

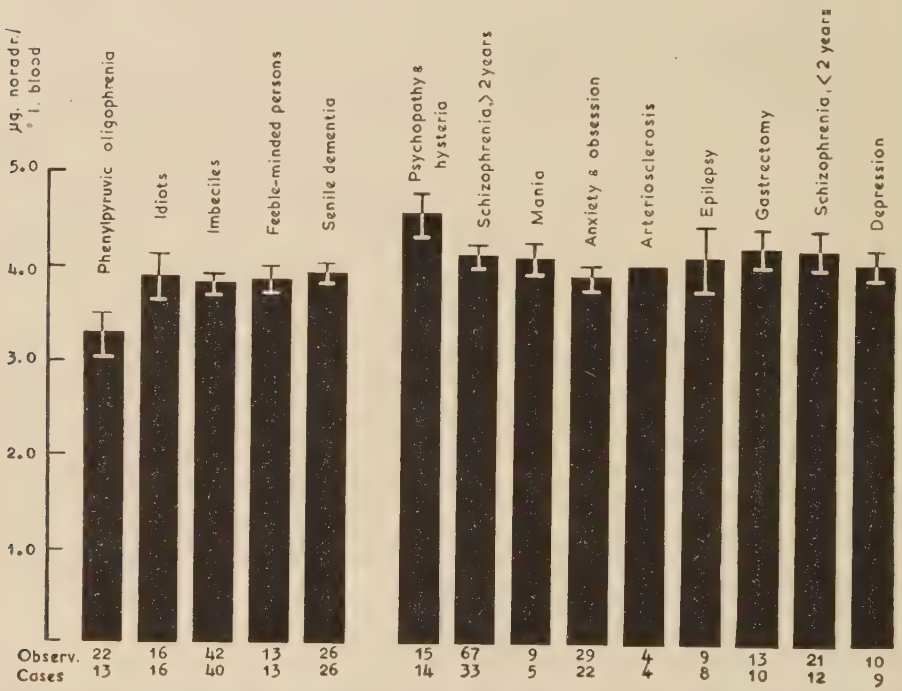

FIG. 16.—Mean plasma-noradrenaline concentration in various groups of oligophrenic and non-oligophrenic patients. The barred lines indicate the standard error of the mean. (Data of Weil-Malherbe, 1954a.)

Summary and Conclusions

The results described in this review seem to indicate a broad correlation between the plasma-adrenaline level and the level of consciousness or the extent of nervous activity. Anaesthetics and relaxing agents lead to a drop of the adrenaline level, sometimes within a minute of the injection. The plasma-adrenaline level is also depressed during natural sleep. On the other hand, the return of consciousness at the termination of hypoglycaemic coma coincides with a peak of the plasma-adrenaline concentration. Electrical stimulation of the brain, the injection of a convulsant drug, or photic stimulation in a susceptible subject, produce a great rise of the plasma-adrenaline level, even if convulsions are suppressed. Finally, the lowering of the adrenaline level in oligophrenia of different aetiology suggests that it is a symptom of the reduced mentation processes in these patients.

Acknowledgments

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ROSTRAL LEUCOTOMY: A REPORT ON 240 CASES PERSONALLY FOLLOWED UP AFTER 1½ TO 5 YEARS

By

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CORTICAL undercutting, as an alternative to standard leucotomy and to the major operation of topectomy, was devised by three surgeons independently. Scoville (1949) published his preliminary results soon after McKissock had begun to do rostral leucotomies. Both have continued to use this type of operation (Scoville *et al.*, 1951; Scoville, 1954) but Ferey (1950), the third to develop a similar technique, was disappointed with the results and soon abandoned it (Ferey, 1953). McKissock (1951) reported the initial impressions of the results in 100 cases and by the end of 1952 had operated on 240 cases. During 1953–54, 1½ to 5 years after operation, I followed up these patients, visiting 175 of them in their homes, and 35 in hospital. Personal follow up was refused or for some reason impracticable in 17 cases, including 4 whose case notes had been destroyed; 13 others had died before the survey was made.

Partridge (1950) reported a follow up study of 300 cases operated on by the same surgeon by his "standard" technique (McKissock, 1943); he had the advantage, which I had not, of being able to see his patients before operation. I have had to work retrospectively, and the case notes available, whilst often excellent, had usually not been made with the idea that they would be needed for follow-up purposes. I have not, therefore, thought it right to draw more than broad conclusions from this study.

I considered using standardized psychological tests but it was clear, from the lack of adequate testing before operation in all but a minority and the slightness of the personality changes in the majority, that none of the relatively crude psychometric techniques at present available could have measured such changes as were present. The investigation has, therefore, been a clinical one with emphasis on "questions as to how the patient feels, what he can do and what do others think of him?" (Curran, 1952); long informal interviews were held with the patients, their relatives and friends, along lines which Partridge used so successfully, and case records were obtained from all hospitals to which patients had been admitted. Most patients were seen only once, but the interview was continued as long as useful information was forthcoming, usually about 2 hours but sometimes much longer; more than one visit was made when necessary. Only 3 brains have reached a neuropathologist and since all of these came from patients who died as a direct result of operation, no information exists as to the extent of the lesion in patients who have recovered.

Most large series of patients reported in the literature contain a majority of schizophrenics; less than 10 per cent. of leucotomies have been done on psychoneurotic patients, mostly obsessional; another 25 per cent. had affective disorders, 60 per cent. were schizophrenic (Kolb, 1953). The corresponding figures in this series are, obsessional and other neuroses and psychopathies 43 per cent., affective disorders 32 per cent., schizophrenia 15 per cent.

The original open rostral operation (McKissock, 1951), here called O, was done in 63 cases: an incision 1 to 2 cm. wide was made below the superior frontal cortex, isolating part of Brodmann's areas 8, 9 and 10. In the next 116 cases a blind incision was made in the same plane or a little posterior to it, using a brain needle; this operation is referred to as B. The plane of operation in the last 60 cases is somewhat different and McKissock (1954) has given this account of the operation he calls G, after Grantham (1950) who introduced a technique for coagulating the inferior medial quadrants of the frontal lobes:

For the original rostral leucotomy burrholes were made just in front of the coronal suture, whereas in this modification the burrholes are made some 5–6 cm. forward of the coronal suture, 2 cm. lateral to the sagittal suture. When the dura has been opened a brain needle is inserted downwards to strike the orbital plate at the junction of its middle and posterior thirds, considerably further back than in the original rostral operation.

The line of section thus runs from above downwards and possibly somewhat backwards in comparison with the original rostral cut which ran from above, downwards and forwards to the junction of the middle and anterior thirds of the orbital plate.

The width of the section of white matter is the same in the two operations, about 2 cm. broad at the lower end of the plane of section, diminishing as it nears the site of insertion of the brain needle superiorly.

It was hoped that by concentrating on the inferior medial quadrants, which Fulton (1951) regarded as so important on experimental and theoretical grounds, and the importance of which has recently been stressed by Sargant (1953), the operation could be made even more effective than O and B; in fact the incidence of the lesion in all three operations should be greatest in the inferior medial quadrant, where the G cut is more posterior than B which in turn is usually more posterior than O.

There has been no agreed way of recording the results of leucotomy. Part of the difficulty arises because the object of therapy differs in different series of cases. Many leucotomies are done to bring about "administrative improvement" (Hoch, 1953), but in the patients considered here the operation was usually done with the hope of restoring to something like normal health. Ström-Olsen and Tow (1949) considered their cases under 5 headings: the result of operation on illness, social status, work adjustment and capacity for pleasure and the presence of adverse personality changes. Wherever possible I have rated patients on a 5-point scale under each of 6 headings, 3 of which show the effect of operation on illness and himself and 3 reflect social adjustment. The rating is given after considering carefully the pre- and post-operative history, taking into account what the patient was before illness and the extent to which his illness incapacitated him.

A patient who is quite unchanged by operation will, therefore, rate SPEWCH 424444, the arithmetical sum of which is 22; one who is slightly improved all round and has no personality deficits will rate 323333, totalling 17; one who is much improved all round and has only slight personality deficits rates 232222, totalling 13; complete restoration to previous normal rates 121111. I have regarded as a good result a total of 13 or less, however derived, as a fair result a total of 14–17 and as a poor result anything more than 17. This has meant that most patients who remain in hospital rate as poor results even when there are real gains from operation; for example, a 69-year-old man, brought after 24 years of unchanging depression to a state of cheerful hypomania,

TABLE I

The Rating Scales

Scale		1	2	3	4	5
S	Symptoms	Free	Much improved	Improved	Not improved	Worse
P	Personality deficit	On balance resulting in improvement	None or indefinite	Slight	Marked	Severe
E	Enjoyment	Fully restored	Much improved	Improved	No change	Less
W	Work adjustment	Up to best previous level or better	Much improved but less skilled or lighter than best previous	Working but efficiency still impaired	No change	Worse
C	Community liability	"contributes" as much or costs as little as before illness	Society much better off	Society better off	No change	Society worse off
H	Home adjustment	As good as best previous	Much better	Improved	No change	Worse

rates 242434. This method of rating has proved useful in assessing results and each case record in this paper includes the SPEWCH ratings.

Complications of Operation

1. *Death.* Three patients died within 12 days; 2 were hypertensive and death was due to cerebral haemorrhage and venous thrombosis; the other died of paralytic ileus and acute haemorrhagic pancreatitis; a good deal of bleeding had taken place in the line of section, which was considered, however, insufficient in itself to have caused death. Two of these patients had had open operations, suggesting that the securing of haemostasis under direct vision is by no means so certain as its advocates believe. There is thus 1 death in 177 consecutive blind rostral operations (0·6 per cent.). Ten other patients had died before the time of follow up, mostly of conditions unrelated to their psychiatric illness, but 3 who were suffering from tension states committed suicide between 1 and 2½ years after unsuccessful open operation.

2. *Cerebral haemorrhage* sufficient to produce focal neurological signs occurred in 4 cases and 2 of these have severe personality deficits. There was less serious haemorrhage in 3 others. In 20 other cases there was confusion sufficient to be noted, or unusual post-operative inertia. Urinary incontinence in the early post-operative period, so common after standard leucotomy, was noted in 22 cases, including 3 of the 4 known to have had major intracerebral haemorrhage and 10 of those who showed undue confusion or inertia. Of the other 9 cases, 2 were incontinent only once, 2 had been incontinent for a long while before leucotomy, 1 was an epileptic who had been occasionally incontinent ever since childhood, 1 was over 70 and hypertensive; 1 had more striking personality changes, which may be taken to indicate a more extensive lesion than usual. Post-operative urinary incontinence, confusion or inertia, in the absence of obvious contributory causes, strongly suggests that the operative lesion has been unduly extensive or has been increased by haemor-

rhage or venous thrombosis. In no case did incontinence persist longer than about 6 weeks without obvious reason. Increased frequency of micturition, usually with slight urgency, persisted at the time of follow up in 14 cases, only 2 of whom had been incontinent. In none was it more than slightly inconvenient.

It has already been noted that 2 of the patients who died were hypertensive. Fifteen others were known to have been hypertensive and the operation had no lasting effect on the blood pressure. Two of the 15 cases probably suffered some unplanned increase in the lesion as the result of bleeding but the clinical results were good in about half the cases. Hypertension should not, therefore, be regarded as necessarily contraindicating leucotomy, a conclusion in general agreement with that of Le Beau (1953) who does, however, regard hypertension and advanced age, above all in combination, as the main contraindications for psychosurgery.

3. *Osteomyelitis* necessitated the removal of bone discs, which had been replaced after open operation, in 2 cases. In one other case a frontal lobe abscess responded to aspiration and penicillin treatment.

4. *Epilepsy*. Two hundred and twenty patients were alive more than 18 months after rostral leucotomy, of whom 4 had previously had standard leucotomy as a result of which 1 was already epileptic. Six were known to have had epileptic fits at some time in their lives; only 2 of these had any fits after operation. Of 15 patients who certainly or probably had intracerebral complications, 3 had fits; one was in status epilepticus on the third post-operative day, but had no fits thereafter. The other 2 had many major convulsions. During the follow up period of the remaining 196 patients, 10 had one or more epileptic fits: 2 had a single fit within the first 5 days; 4 had single fits between 12 and 26 months after operation, one of whom was, by that time, in a state of advanced arteriosclerotic dementia. Two patients had attacks of status epilepticus 14 months after operation.

Twenty-three patients later had a second operation, 2 of whom had already had fits after the rostral operation. Of the remaining 21, 5 subsequently became epileptic. Thus the incidence of epilepsy after uncomplicated rostral leucotomy is 4·6 per cent., a lower figure than after any leucotomy except transorbital, when the incidence is about 1 per cent. (Freeman, 1953). Intracranial complications or more than one operation raise the incidence to about 22 per cent. Freeman, too, has reported greatly increased incidence of epilepsy under similar circumstances (53 per cent. of 54 cases submitted to more than one standard operation). There is no evidence in this series that the incidence is higher among men (as Stengel, 1950; Partridge, 1950; Freeman, 1953, found), or in schizophrenics (as Stengel and Partridge but not Freeman found).

Few patients took the phenobarbitone recommended as a prophylactic against epilepsy: the incidence is so small and severe epilepsy so rare that there seems no need to prescribe phenobarbitone unless intracranial complications or more than one operation make the risk of epilepsy more considerable.

5. Apart from post-operative mania, discussed below, the only notable psychiatric complication of operation is marked disinhibition which may necessitate heavy sedation and a side room; this was noted in 6 patients, 4 of whom were obsessionals. It is likely that others were similarly, though less markedly, disinhibited. The noisy phase lasted up to several weeks and appears to correspond to the post-operative syndrome which Le Beau (1952) and Klein (1952) referred to as hypomanic, and which the former relates to damage to Brodmann's area 9.

In the absence of obvious causes, such as operative haemorrhage resulting

in a larger lesion than usual, personality changes following rostral leucotomy are slight. I am dealing with them in a separate paper and it suffices to say here that they are similar in kind to those observed after standard leucotomy and to those described by Tow and Whitty (1953) after cingulectomy, but are much less than after standard leucotomy and negligible in all but about 5 per cent. of cases symptomatically improved. A comparable figure after standard leucotomy is 56 per cent. (derived from Partridge, 1950).

Apparently distinct from post-operative disinhibition which diminished within a few weeks of leucotomy, is a phenomenon which Partridge observed but which has appeared much more frequently in this series; 10 patients operated on for depressive illnesses have had attacks of hypomania only since operation. Seven cases occurred in 18 patients regarded as suffering from recurrent endogenous depression who had had their first breakdown before the age of 40.

In one case it did not happen until over a year after an apparently ineffective leucotomy and it seems unlikely that operation had anything to do with the mild hypomanic state which then occurred. In 2 cases, men of 54 and 62, the change followed directly on operation and has persisted despite subsequent standard leucotomy, which has increased the personality deterioration and merely damped down the hypomanic manifestations. In another the 9 months of elation made home life enjoyable for her family as well as herself and only subsequent progression of arteriosclerotic dementia made hospital care necessary. A woman of 65 had suffered from cyclothymic mood swings all her life and in the 21 years before leucotomy had had 7 severe depressive breakdowns. E.C.T. at these times produced an irritable, shortlived elation but for 2 years had been ineffective. After leucotomy her mood swings occurred from a higher basic level, so that the depressions, which still occurred regularly, were less deep and alternated with a "champagne mood", in which she was interfering, quarrelsome and given to abusing her husband. On the whole, however, this was preferable to her pre-operative state. In yet another case, a man of 48, who for many years had been mildly depressed for a few weeks in each year, became more steadily depressed, ruminative, irritable and indecisive. After leucotomy the periodicity gradually changed and 18 months later his mood varied between depression and elation at intervals of a few days, with no intervening normal periods.

One of 21 patients operated on for involutional depression was described as paranoid and hypomanic for about 2 months after operation and then recovered; it seems possible that this was more like the "disinhibition" described above.

Two of 5 non-involutional patients operated on during their only depressive illnesses became hypomanic and another became hypomanic for several months, more than a year after standard leucotomy had been done as a second operation.

One had always been a forceful, dominating personality and for the 18 months his hypomania lasted became impossibly overbearing; the other was a morose, inhibited, unsociable leptosomatic individual of 44; he had always wanted, so it was noted before operation, to be a hypomanic business man, achieved this ambition some 4 months after leucotomy, and during the 5 months it lasted got into difficulties from which he has not extricated himself a year later, for he put up virtually the whole of the capital in an unsuccessful business venture with a convicted embezzler, though in fairness it must be said that the failure was not the fault of the latter. The characteristic hypomanic press of activity was well shown in his efforts to pack for the summer holiday; he broke off repeatedly to do unimportant repairs to all the door knobs in the house and when, 48 hours late, the family eventually reached the seaside, he was found to have packed an immense quantity of unnecessary things into the car, even including the telephone directory. Whilst on holiday he organized a large midnight fishing expedition, but omitted to arrange for a boat to be available. When he returned home he gave considerable financial support, which he could ill afford, to a new theatrical company, and bought most of the seats for their first performance. This meant that many people were unable to get in, and since he omitted to find anyone to use his tickets the first house was almost empty.

No case of hypomania occurred in any other diagnostic group and it seems clear that the risk is only considerable in cases of affective disorder which belong with the manic-depressives, or at any rate cannot strictly be regarded as suffering from involutional or neurotic depression. In such cases there has been an incidence of 8 in 23, and in the end, though the result has been worthwhile in 4, it has been good in none of the 8.

Rostral leucotomy should, therefore, be used cautiously in cases of recurrent endogenous and non-involutional single depressions; hypomania has not been conspicuous in reports of orbital undercutting for depression (Rylander, 1952; Scoville, 1954) and it may be that this operation will be found preferable for such cases; it is important to take note of anything pointing to a manic-depressive basis for an involutional melancholia, particularly a history of a tendency to depression or a positive family history, e.g.:

A 62 year old irritable, extraverted merchant had no breakdown until he was 60 except for 2 brief and minor depressions after influenza. He was a conscientious man, on good terms with everyone and "a born wit"; his father had been a well known local public figure; 1 brother had committed suicide, another had been in a mental hospital and a third, the black sheep, had been exported in youth. In a severe agitated depression at 60 he believed his business had gone to ruin and made several suicidal attempts. E.C.T. brought only temporary relief. After leucotomy he became elated, boastful, arrogant, extravagant, sexually demanding, and drank to excess. After 9 months of persistent hypomania a standard leucotomy was done with resulting severe frontal lobe deficit but no change in mood. Fifteen months later he was deteriorating physically and mentally, but was still hypomanic.

Results

Consideration of the results of the 3 types of rostral leucotomy, O, B and G, is inevitably complicated by the difficulty of comparing one case with another. The criteria for selecting patients differed somewhat for each group; since the O operation could only be done at a neurosurgical centre a majority of the patients were admitted from general hospital out-patient departments or from private practice. The B and G operations, which could be done almost anywhere, were carried out in many hospitals, mainly in Southern England and Wales. Few schizophrenics were accepted until G was introduced and it was thought, partly because of the success of bimedial leucotomy (Greenblatt *et al.*, 1952) that it might prove an adequate cut. The initial impressions (McKissock, 1951) have been confirmed: in no diagnostic category does the O operation give as good results as the others; there is little to choose between B and G (see Table II).

Table II

Psychoneurotic and Psychopathic States and Affective Disorders (Excluding Manic-depressive Psychosis with Manic Episodes). Results in 160 Cases Surviving Operation, Whose First Operation was Rostral Leucotomy

Type of Operation	Number of Cases	Good	Per cent.	Fair	Per cent.	Poor	Per cent.
O ..	39	8	(21)	6	(15)	25	(64)
B ..	84	41	(49)	16	(19)	27	(32)
G ..	37	16	(43)	8	(22)	13	(35)
Total ..	160	65	(41)	30	(18)	65	(41)

In other words B and G have given good results in nearly 1/2 the cases selected in these categories and fair results in another 1/5, or 2/3 altogether, whilst O gave good results in 1/5 and worthwhile results in only 1/3 altogether.

There is some evidence that intellectual damage is likely to be more marked after G than after B, perhaps because any unplanned extension of the more posterior G lesion may be expected to isolate more frontal lobe than a similar extension in the plane of B. The B operation is therefore recommended as the most satisfactory of the three rostral operations.

It is now generally accepted that the most noticeable effect of a successful leucotomy is the relief of emotional distress. Not all tense patients are relieved of illness but patients who are not tense are rarely helped. Sargant (1953) stated that symptoms which are secondary to emotional tension are likely to be relieved and in this series this general conclusion is confirmed, whether the symptoms are hysterical, obsessional, aggressive, etc. Depression is often relieved at once, but patients who had been several years in hospital responded less quickly and the behaviour of 2 continued almost unchanged until something happened to jolt them out of their ruts; both had been more than 5 years in hospital for involutional melancholia and seemed to settle back again into their customary patterns of behaviour; in one case the illness of her husband provided sufficient stimulus for her to leave hospital and to resume the management of her household.

The results in the different diagnostic categories are shown in Table III. (Figures in parentheses, other than percentages, exclude those who had open operation.)

TABLE III

	Good	Fair	Poor	Total	Operative Deaths
Affective disorders ..	35 (49%)	14 (20%)	22 (31%)	71 (61)	
(*a*) Cases with both manic and depressive attacks		1 (1)	3 (2)	4 (3)	
(*b*) Recurrent, mainly endogenous, depression ..	10 (10)	5 (3)	7 (4)	22 (17)	
—with dementia ..		2 (1)	2 (2)	4 (3)	
(*c*) Recurrent, more reactive depression	10 (9)	2 (2)	3 (2)	15 (13)	
(*d*) Single depressions:					
(i) Involutional ..	14 (13)	2 (2)	4 (4)	20 (19)	
—with dementia ..		1 (1)		1 (1)	
(ii) Non-involutional ..	1 (1)	1 (1)	3 (3)	5 (5)	
Psychoneuroses and Psychopathy	31 (34%)	17 (18%)	47 (49%)	95 (65)	
Tension states	11 (8)	10 (8)	12 (6)	33 (22)	
Obsessional states	12 (10)	4 (4)	10 (6)	26 (20)	
Hypochondriasis	3 (2)	1 (1)	9 (5)	13 (8)	1
Psychopathic personality ..	5 (5)	2 (1)	16 (9)	23 (15)	
Schizophrenia and paranoid illness	4 (13%)	5 (16%)	22 (71%)	31	1
Mental illness in reaction to or in association with organic disease	9 (45%)	2 (10%)	9 (45%)	20	1
Unilateral		1	6	7	
Untraced				13	
				240	

Affective Disorders

The results (see Table III) compare favourably with those obtained by more extensive operations.

(*a*) Only 4 patients had both manic and depressive attacks before leucotomy and the only one to derive any benefit was relieved of a depression which had lasted a year, but, to quote her employer, "she went into hospital like a lamb and came out as a dragon". Three years later, having passed through a post-

operative hypomania, she was drifting from one casual ward to the next (particularly favouring one which gave her a Chelsea address), verminous and cheerful and occasionally bothering her family when short of money; psychopathic traits, previously present, had been exaggerated. On the whole rostral leucotomy is not advised for this category of patient.

(*b*) The particular risk of hypomania in cases of recurrent endogenous depression has already been emphasized; nevertheless good results were obtained in nearly half of these cases, and fair results in another quarter (excluding those who were already showing signs of organic dementia). Depression was relieved in 5 dementing patients but good results were marred by unpleasant personality changes accompanying the dementia; it is important to warn relatives of this since otherwise they may reproach themselves with having sanctioned the operation.

(*c*) The group called "recurrent, more reactive depression" consists of 15 vulnerable personalities readily cast down by minor setbacks and retaining some symptoms between more serious breakdowns which in nearly every case necessitated repeated admissions to hospital, e.g.:

A timid, obsessionally slow and fussy spinster of 49 had had, fortunately for her, no need to earn her living, but spent most of her time looking after her foster father. For 3 years from 35 she was receptionist to a doctor, to whom she grew greatly attached, and when it was no longer possible to continue working for him she became worried and depressed; for 11 years she was repeatedly in this state in reaction to even slight stress, each time recovering with E.C.T. or cessation of the stress. Leucotomy was done to interrupt this pattern and was successful: there had been no recurrence in 2½ years after operation, but her irritable, abrupt and outspoken manner earned her the reputation of being aggressive and she lost a job because of it. Sensorial testing suggested slight intellectual impairment, but few demands are made on her as companion to an older woman and this is not evident in her daily life. (131312)

Ten of the 15 were good results. The 2 poor results had such inadequate personalities and (for them) such overwhelming and unalterable problems that it must be doubted whether the decision to operate was wise.

One 37 year old man was quite unfitted for the responsibility of earning for his wife and 4 children and for the burden of a heavy mortgage on his home: as his wife said, he would have made an ideal lodger, but he was a hopeless father. (334344)

The 3 fair results were less than good because of personality inadequacies, and in one case because a tendency to depressive mood swings persisted.

(*d*) The best results were in the group of involutional melancholics, with 70 per cent. good and another 10 per cent. fair. They had been ill for between 6 months and 9 years; length of illness only seemed of importance in that recovery was slower in those who had been more than 5 years in hospital. Of the 4 poor results, one was almost symptom free for 6 weeks but relapsed and was then allowed to become institutionalized; one failed to derive any benefit from a later standard leucotomy; one recovered after a series of spontaneous epileptic fits a year after operation. The fourth relapsed within a few months. These results are similar to the half–three-quarter good results generally reported after standard or lower quadrant operations in affective disorders, and in view of the lesser personality changes after rostral leucotomy suggest that this operation might well replace the others, especially in cases of involutional melancholia and reactive depression.

Tension States

Curran and Partridge (1952) referred to a group of "undifferentiated tension states"; try as I will, I cannot usefully subdivide this group into more diagnostic categories. Most but not all are vulnerable personalities, retiring,

unassertive people, who have remained immature and dependent. The home background in many cases is grim; they have found little security with their quarrelsome parents, overpowering, neurotic, physically incapacitated or otherwise unsatisfactory mothers and intense sibling rivalries; at best their adjustments are precarious and their psychoneurotic reactions to any stress are diverse; along with tense anxiety and its somatic expression in headaches, sweating, flushing and a host of other symptoms, they are often depressed, hypochondriacal, ruminate obsessively, or exploit symptoms for gain in an hysterical way. Phobias are frequent and in a few dominate the clinical picture. Symptoms tend to alter from time to time in response to treatment or changes in environmental circumstances. Many were treated by physical methods and psychotherapy, with temporary restitution of the unstable adjustment. Not all patients were as inadequate as this description would imply, and the more adequate personalities seemed on the whole to do rather better than the inadequate.

A particularly good result was a 33 year old sociable, extraverted woman, a hairdresser, who had separated from her psychopathic husband just as her mother before her had separated from her drunken father; she became tensely depressed and derealized, with obscene obsessive rumination, when deeply attached to a man with whom her rigid, convent-derived moral principles would allow her no intimacy. Though E.C.T. lightened her depression her life continued to be intolerable because of her ruminations; open rostral leucotomy was done after an illness lasting only 8 months. Tension was immediately relieved and she gradually stopped ruminating during the next 6 months. Three years later she was well and leading a full and happy life. Beyond a greater readiness to relax, in her case a good thing, and a slight increase in outspokenness, not in the least offensive, no personality changes had been noticed. (131111)

Another good result was a 47 year old builder, with a background of poverty and drunken, quarrelling parents. He was a compulsive worker, whose stability had depended on his devoting every scrap of energy to his work, and had been described as a human dynamo. He had, in fact, been tremendously productive, but when short of work readily became hypochondriacal. The death of his wife imposed a severe strain on him and when, a few years later, he had a colonic resection for carcinoma a severe tension state developed, in which he became obsessed with religion and had several ecstatic experiences; at one time he was considered paraphrenic. Leucotomy relieved tension but with it went much of his abnormal drive, so that he is now a shadow of his old dynamic self and no longer minds having lost his zest for work. The scale of his building operations can now be measured in tens of thousands of pounds instead of in millions. (232222)

The result was fair in the case of a 45 year old clergyman, an indulged only child, whose reaction to stress had always been to develop somatic symptoms and hypochondriacal concern over them. His leucotomy was done after increasingly severe tension in the face of real parochial troubles had made it difficult for him to carry on during 4 years. Some relief of tension was obtained and he returned to his parish within 10 days of operation, where he has since carried on although his symptoms have been exacerbated as fresh problems have faced him. (323123)

The next case is an example of the effect of leucotomy in a less adequate personality:

A married woman of 25, two of whose sisters were similarly shy and sensitive, had always been upset by quarrels between her parents. Easily embarrassed and acutely conscious of blushing excessively she had, on this account, to leave the Land Army in which she was working happily. After some conflict and indecision she married and was obsessionally houseproud, fearful of going out and of meeting strangers. Despite out-patient psychotherapy she continued to be intensely self-conscious and variably depressed and after 3 years was leucotomized. For a year she was better, but the attempted suicide of a neighbour threw her into a panic and she has needed regular sedation since to control recurrent attacks of panicky and guilt-ridden depression which are, however, becoming less frequent. Two and a half years after operation her husband says "for the last 6 months I have known what it is like to have a normal wife"; but she still has some symptoms and has suffered some intellectual loss of which she is well aware but does not regret. She is more irritable and has less endurance, but her lessened concern with appearances makes her easier to live with and the reduction in emotional tension makes her more stable. (232211)

This case illustrates well the way in which personality deficits common to many patients after leucotomy can, in a particular personality setting, lead to both undesirable and desirable effects. There is a worthwhile relief of tension but less than one might expect from a standard leucotomy: on the other hand personality deficits are only slight and satisfactory relief has been achieved without undue "simplification" of the personality.

In the group of 33 patients with tension states, 11 rate good results, 10 fair and 12 poor. The reason for failure was not always clear, but one hysteric, comfortably resident in a mental hospital seems to have been mistakenly regarded as tense. Six patients later had more psychosurgery and 4 were symptomatically helped, but in all but one, who had a unilateral standard operation, the personality deficits were such as to make them in many ways unsatisfactory people. I am discussing the question of second operations in another paper.

Obsessional States

Ten of the 26 cases resembled those discussed under the heading of Tension States but the obsessional features were more marked. Four rate as good results, 3 as fair and 3 as poor. Two of the poor results were in markedly immature and insecure young women, with overwhelming dependent needs, features which seem to make it impossible for patients to take advantage of the general reduction in tension brought about by operation. Both these patients had to cope with unaltered environmental conditions which were full of conflict for them:

A woman of 34, terrified in childhood by constant quarrels between her overbearing and aggressive mother and her cyclothymic father, felt herself inferior to her more favoured older sister and was a cowed, enuretic, much punished child, who early developed obsessional rituals against her fears. She was further handicapped by recurrent attacks of acute rheumatism and was dyspnoeic from mitral stenosis. Her mother and sister interfered in her marriage and her husband demanded fellatio. Though partly relieved by leucotomy of the depression which had totally incapacitated her for a year she remained immature, insecure and still had obsessional ruminations and compulsions. (324423)

In 5 cases entrenched ritualistic behaviour was the most striking feature and the only one who was even a fair result has frontal lobe deficit symptoms more marked than in any other patient in the series, except some of those who had extensive cerebral haemorrhage.

One woman, the daughter of an obsessional, neurotic mother, had compulsive symptoms for 16 years, but these had only become crippling for 3 years, during which she used them in a never-ending hysterical vendetta against her husband for his supposed infidelity. All that leucotomy did was, to her annoyance, to diminish her energy; she was liable to drop off to sleep in the midst of her compulsive cleaning, so that she could achieve less in the time. Three years later the disaster she had both feared and courted came about, for her husband left her. (434444)

In 4 men of markedly obsessional personality and with predominantly ruminative symptoms from childhood, the essential pattern was unchanged by leucotomy but reduction in intensity of symptoms, whilst accompanied by no striking change in the way of life, was such that 2 rate as good results and one, though he remained in the grip of a tyrannical routine, has lost the somatic symptoms of anxiety which previously accompanied frequently recurring depressive phases.

In 5 cases in which the onset was more definitely related to specific external events the result was good.

A 32 year old woman of low average intelligence grew up in a broken home with a mother who was "always on about germs". She had no obsessional symptoms herself until at 24, 3 days after her marriage, a former boy friend turned up and she was involved in regrets and doubts, which found expression in fears of contamination and elaborate protective behaviour, particularly against contamination by anything which came into the house by post and which seemed to symbolize the desired but rejected suitor. During the next 8 years the spread of obsessional behaviour progressively crippled the whole family. After rostral B leucotomy it gradually died away and when, a year later, her husband became incapacitated for work, she found it possible to work as a bus conductress. In the past, because of her fear of contamination by money, this would have been impossible. Those few symptoms which remain are easily tolerated and she and her family are delighted. (232111)

The 2 remaining cases present marked psychopathic features:

A 27 year old typist had indulged in sadistic masturbatory phantasy from the age of 3, and her childhood was marked by ritualistic confessions, prayers and expiatory rituals. She was immature, and though superficially kind and considerate this was a cover for much hostility. She "liked to think up all the naughty things and make someone else do them", and later tried many times to bring about her mother's death by making her go up and down stairs unnecessarily, hoping her heart would fail, or by screening her from approaching traffic, only to step back suddenly leaving her mother as a target. She was preoccupied with thoughts of food, and as a result of compulsive prohibitions and phobias came to resemble a case of anorexia nervosa. Leucotomy made her euphoric and 3 years later she clearly got immense fun from her life. Release from compulsive restraint enables her to indulge a perversion of eating reminiscent of the orgies of the Roman decadence, but since this is carried out late at night and in private and her behaviour otherwise is entirely satisfactory the result cannot be regarded as other than good. (231111)

The other case was referred to by Maclay (1953) as the third of 3 people who have committed murder after leucotomy and are now in Broadmoor.

She had an operative haemorrhage and her obsessional symptoms were greatly relieved for 9 months thereafter. It is debatable whether leucotomy can be held in any way responsible for the "suicide pact" with her young daughter, which resulted in the latter's but not her own death. Her personality was such that had anything like this occurred apart from leucotomy, it would not, perhaps, have been really surprising.

The cases of obsessional illness in this series were probably rather less severely incapacitated on the whole than in Partridge's (1950) series. Table IV compares the results in obsessional states with Partridge's, using his terms to describe the improvement.

TABLE IV

	Partridge (1950) (24 cases)	Rostral Series (26 cases)	
Operative death	1	–	
Non-fatal haemorrhage, final result worse	–	1	
Unimproved	1	3	"Poor"
Slightly improved	1	6	
Distinctly improved	1	4	"Fair"
Substantially improved	9	9	
Relieved of obsessional symptoms altogether	11	3	"Good"

Evidently rostral leucotomy is less effective in relieving symptoms, but the results are satisfactory, particularly in those cases with marked tension who resemble the patients discussed under "Tension States", and those whose illness has been related to specific environmental stress, especially if they were not previously grossly obsessional. The worst results, as with all psychosurgery, were in those with entrenched ritualistic behaviour and those whose obsessional behaviour was hysterically motivated. The more a compulsive act comes to resemble a conditioned response, carried out automatically, the more likely is it

to persist, just as delusional beliefs and phobias may persist; it may be, as some of these cases suggest, that fear which has become conditioned to a situation, such as travel, which provides a real and continuing stimulus, is less likely to be relieved than a phobia which arises more directly on a basis of emotional conflict. Thus, for example, a young obsessional had two main fears:

(*a*) that he had somehow infected girls with syphilis (this did not apply to any particular girl, and seemed based on masturbatory guilt).

(*b*) that he had left engines, on which he worked, in a dangerous condition. The first fear was relieved by rostral B leucotomy, the second, the conditioned stimulus for which was ever present, was not.

Often the intensity of experienced fear was much reduced in the feared situation (e.g. travelling) if patients could be induced to face it, but in several cases the phobia continued to be just as incapacitating because patients would not put themselves to the test.

Hypochondriasis

As a symptom this is common enough in depressive, schizophrenic and psychoneurotic states in general. Here are considered 14 cases in which preoccupation with supposed physical ailments or excessive concern with real physical illness dominated the clinical picture. Apart from one case in which hypertension, abnormal EEG, dilated ventricular system and psychological tests suggested an organic basis for involutional hypochondriasis, all were suffering from hysterical illness in that their symptoms, however unsatisfactorily, provided some solution for life problems of which they were more or less aware but did not connect, at any rate fully, with their complaints. One died of operative haemorrhage; in two, depressive features were evident but had become obscured by marked hysterical features; both of these did well:

A dull and envious woman of 41 had haunted her doctor for 17 years with hypochondriacal complaints, mostly about her bowels. An epileptic and mentally defective daughter was part of the life problem behind her symptoms. At 40 the departure of her son overseas on national service precipitated a depressive illness with early waking, weight loss and diurnal variation of mood, in which her hypochondriacal complaints were magnified. In the course of a year the depressive features faded and it was for the persistent intense hypochondriasis and despite 'belle indifférence' that leucotomy was done. She is not symptom free but much less concerned over her health and no longer broods so jealously. Nearly 4 years after operation she was again depressed for a few weeks when her son's good fortune in being given a new house made her envious, but this passed with the help of a bottle of medicine. (232221)

Amongst the 11 other cases there is only 1 good result:

A 65 year old woman whose miserable preoccupation for many years with facial pain seemed related to a not entirely satisfactory relationship with her husband. Despite this she had a good home and after operation seemed more able to accept the comparative emptiness of a life in which "so long as I take my dog out my day is full". (232112)

An important distinction between this case, which did well, and those who did badly, seems to be the degree to which a life problem is overwhelming a particular personality. In the case of a 52 year old man who had also complained bitterly for years about facial pain, which had begun as trigeminal neuralgia, the life problem was a squalid home with a wife who was an outspoken slut. Relief of his symptoms would necessitate making him insensitive to his surroundings and to the pride and insecurity which made it impossible for him to get rid of his wife. I do not think that standard leucotomy would do any better in this case, but rostral leucotomy certainly had no obvious effect. In the other cases, too, symptoms seem necessary in the sense that life has set problems which these personalities cannot tackle in any other way. There is, for example, a woman

of 58 left with tinnitus by a labyrinthine haemorrhage, who after receiving an unhopeful prognosis said, "I am not going to be a deaf old woman. This means another breakdown for me." Since her hypochondriasis brought her a great deal of loving care from her husband it was not surprising that leucotomy failed. Rostral leucotomy has, in fact, been conspicuously unsuccessful in cases of hypochondriasis. This contrasts with the common opinion that cases of hypochondriasis do well with leucotomy and the reason lies, I think, not in rostral leucotomy being an inadequate operation, but that many cases were wrongly selected, who had adopted hypochondriasis as a way of life with which they could not dispense. Where hypochondriasis is symptomatic of depression, where there are personality assets and a possibility of altering an unsatisfactory environment then much better results can be anticipated. One patient illustrates very clearly the relief of emotional illness but with persistence of a hypochondriacal way of life.

An actress of 50 had never really achieved anything so satisfying in her life as playing in Maeterlinck's *Blue Bird* at the age of 8. A lifetime of hypochondriasis, with frequent visits to hospitals in two continents, had given her life some meaning and provided excuses for not having done better in her career. When her mother died she became agitated and depressed and her hypochondriasis assumed tremendous proportions. With the relief of depression by open rostral leucotomy a year later she reverted to her normal level but was perhaps more difficult to live with because of an accentuation of her shrewishness and an increase in absentmindedness. (132322)

As judged by these results *the indication for leucotomy is not hypochondriasis, but tense, anxious hypochondriasis.*

Psychopathic Personalities

There is no sharp distinction between the many vulnerable personalities considered under other headings and the 23 patients discussed here. There is, however, in these a more marked lack of restraint in behaviour, a greater impulsiveness, egocentricity and lack of thought for others; many could be called sociopathic. Some were unrestrainedly aggressive and in 7 the operation was done largely because of this; only one of these was even a fair result and there is reason, from the marked personality deficits, to suspect an unusually extensive lesion in her case. Of 5 inadequate psychopaths only one rates even fair and this because he was relieved of compulsive behaviour based upon obsessional rumination.

An alcoholic with a consumption of 30 pints of beer daily had always been intolerant of discipline and several times in the hands of the police for aggressive behaviour; since operation he drinks as much, is even less restrained and on the whole worse. (434445)

A young rag and bone man, from a squalid East End home, had for 3 years been incapacitated by a severe tension state following a motor smash when on unauthorized absence from his unit in the army. Rostral B leucotomy only relieved tension for a few weeks. Within 2 months of operation he had become actively homosexual and one must assume that leucotomy had some effect on bringing this about though even without it would not have been an unexpected development. (424444)

Two schizoid psychopaths became more stable and rate as good results; these and the 3 good results in cases of psychopathy with marked hysterical features are clearly related to relief of tension; in each case antisocial behaviour was dependent on intense suffering; in the 6 cases of hysterical psychopaths who did poorly it was much more evident that they had never learnt to discipline feelings or restrain their impulses; in 4 there was a purposive use of symptoms which was less evident in the others considered in this section. None of 4 patients who had a second operation was any better for it and one was very much worse.

Twenty-one patients were operated on for *mental illness as a reaction to or in association with organic illness*. Seven had intractable pain and the findings here were in agreement with the many authors who have written on the subject: leucotomy often relieved emotional distress so that less attention was paid to pain; in one case of postherpetic pain in a recurrently depressed and anxious man, whose pain showed diurnal variation, the depression was mitigated in the way that Stengel (1950) described and in the course of 6 months his pain gradually disappeared. In one case of severe pain following ophthalmic herpes zoster, rostral O leucotomy was ineffective and later standard leucotomy reduced the patient's emotional over-reaction but only at the expense of serious personality deficit. Where pain was an "old friend" (Penman, 1954) and apparently a necessary part of the patient's adaptation to life, leucotomy had little effect e.g. a plump and contented man who for 15 years had done no work because of facial pain, collapses and a host of other hysterical symptoms, and had become comfortably dependent on pethidine and phenobarbitone.

Tinnitus was a prominent symptom in 7 patients and in 5 the operation was done mainly for its relief; 4 of these were included in the group of 17 discussed by Elithorn (1953) and there is nothing to add to his conclusions. Three hypertensive patients, who became depressed in association with strokes, the result of cerebral vascular disease, all did well.

There remain 6 patients suffering from miscellaneous conditions and no useful conclusions can be drawn from the study of them as a group.

Schizophrenic and Paranoid Illnesses

Thirty-two cases, one of whom died as the result of operation. In 2 the rostral operation was done some years after a standard leucotomy had failed to give relief and in one of these, though the final result was poor, the "administrative" improvement was worthwhile. Ten patients derived no help in any way from rostral leucotomy and later standard leucotomy in 4 of them only led to worthwhile improvement in one, a young man regarded, probably wrongly, as a simple schizophrenic, who had had recurrent depressions for 9 years. Eighteen patients were symptomatically improved by the reduction of suffering; 2 relapsed quickly and in most of the others there was no striking change in the clinical picture. In 3 cases, however, there was complete and lasting remission and in a fourth sufficient relief to allow resumption of a comparatively normal life, these 4 patients rating as good results. Two were suffering from paraphrenia which developed in the sixth decade in patients who had not previously been ill.

A methodical, fussy schoolmaster of 65 had for 5 years increasingly bizarre hallucinatory experiences and primary delusions to which he reacted at first with interest and annoyance and later with despair. E.C.T. brought about a complete remission for 10 months. With further recurrence of his unpleasant experiences, which included the removal of his ghost body to a well known teaching hospital at night for experimental purposes, he became depressed and made a determined suicidal attempt. Two and a half years after leucotomy he has remained well and has given no indication to his wife of remembering anything of his illness. He has resumed teaching and the only change in personality is that he is a "little toned down" and less inclined to worry over trifles, minor changes which but for his having had an operation would have been put down to advancing years. (111111)

Complete remission was obtained in a 23 year old girl who had broken down suddenly 18 months before without any obvious external stress. She was agitated, depressed and perplexed, with vivid aural and visual hallucinations and incontinence. E.C.T. always had a temporary good effect in recurrent phases of more intense suicidal depression. Eighteen months after operation she had been working well for a year and was making sensible plans for her marriage. (131112)

The results were regarded as fair in 5 cases, in 2 of whom it is doubtful whether leucotomy played much part. It appears from this small series that rostral leucotomy is only likely to be useful in schizophrenia where there is a good prepsychotic personality; where the affective response is strong and appropriate, tension and depression being especially likely to yield; where aggressive acts and phantasies, if present, are directed against the self rather than outwards; where illness is of less than 4 years duration or episodic or fluctuating markedly in response to environmental influences. Late paranoid and atypical illnesses on the whole do better than other types. In fact, no patient readily classifiable as hebephrenic, simple or catatonic did well, though several had some symptomatic relief.

Discussion

So far I have explicitly mentioned the prognostic importance of emotional tension; this is so in all diagnostic categories (Greenblatt *et al.*, 1953, found it the only clinical factor of definite predictive value in their series of 116 mostly schizophrenic patients).

To have confidence in prognostic criteria derived from a study such as this it is desirable that patients should have been assessed before and after operation by the same observer. In this series it was not possible for me to see patients beforehand and conclusions are therefore put forward tentatively. It has seemed clear that besides the presence of emotional tension and a quantitatively adequate incision (O is rarely adequate) the quality of the result depends upon the personality of the patient and on the sort of environmental difficulties with which he has to cope after operation; it is not easy to judge to what extent environmental difficulties are truly insurmountable for a particular patient; only the history can give some guide and in some cases which have been cited the failure of leucotomy to make these inadequate people more adequate is not surprising. Golla (1946) observed that the operation was to be "considered only as a step in the reintegration of personality". Often too little attention is paid to environmental factors, and leucotomies seem to be done as a last resort without adequate investigation of the problems which will continue to face the leucotomized patient. The results in many cases of affective disorder tend to make one forgetful of the amount of social work and psychotherapy which may be needed before a neurotic patient is in his stride again: many middle aged depressives have good personalities, established homes and loving relatives and, if they have not been ill for many years, little or no rehabilitation is needed after the rostral leucotomy. The situation is very different for psychoneurotic and psychopathic persons whose long partial incapacity has often created problems which may indeed be insoluble. I cite one case at length to indicate the sort of case work which may be needed, and without which it is useless to leucotomize:

A 45 year old housewife, the fourth of the nine children of an improvident drunkard, was brought up in an industrial slum. She was described by her mother as "the worst-tempered child" but got on well outside the home. Obsessional symptoms appeared at 14 and her left hand became, as it were, sacred, so that it could only be used for "good" things. Many rituals developed and lasted for 9 years but were not seriously incapacitating. Recovery was sudden and followed a determination to stop it all; apart from minor obsessional traits she was well until 36 when she had a breast abscess after the birth of her only child. Obsessional rituals increased and she was many times in hospital, depressed, irritable, tense and apprehensive. Finally she was totally incapacitated and she and her home were filthy. No amount of social work had been able to prevent this. Leucotomy made little obvious difference at first and she spent most of the next year in a convalescent hospital where she found she could carry out some actions, such as knitting, which previously had been impossible. Meanwhile an energetic

social worker badgered the local authority into cleaning up the home, so that when she returned she did not have to face tasks which almost certainly would have precipitated a relapse. Social work and support have continued and she has made steady progress. Comparatively minor obsessional symptoms remain but the final result is good. (212122)

Sometimes the changes necessary occur by chance, and the fact that such things can happen should keep us alert to the possibility of engineering helpful changes:

A 23 year old dressmaker had been ill for 4 years with a severe tension state precipitated by fears that her parents were going to separate. She had become emaciated and no treatment (including narcosis, E.C.T., 20 insulin comas and a year of psychoanalysis in hospital) made any real difference. After leucotomy there was little obvious change, but she herself thought she was calmer. She did not leave hospital until 7 months later and then, living with her mother, found herself rapidly reverting to her previous state. At this point she chanced to meet a kindly man, ten years older than herself, who took her around, giving her interests outside her home, and eventually in the face of maternal opposition, married her. Five years after operation she was, with his support, coping well with housing difficulties and had had a baby. The rating 222211, indicating a good result, probably owes as much to the change in her circumstances as to the leucotomy.

The patient who has been long in hospital must not be allowed to settle back into his old ways after operation: the tendency to persist in old habits is shown not only by schizophrenics, but by depressives, phobic and obsessional patients as well.

A 62 year old printer, a prim, fussy little man who had been more than 40 years with his firm, felt himself ridiculed when a question he had suggested to a friend was derided at a political meeting; 2 sons had been killed in the same year; he developed an agitated depression for which he spent 5½ years in hospital before rostral B leucotomy was done. There was little apparent change for over a year until his third son, who had been away on national service, came to see him. This seemed to provide enough of a stimulus to alter his outlook; within a few months he had recovered and went home where his wife, having made a life of her own in the 7 years he had been away, could not abide him and soon left. He is working well at his old job and his associates find little difference in him. (121112)

Several patients improved strikingly as soon as they were discharged from hospital. In general there is no need for prolonged rehabilitation in hospital after rostral leucotomy, provided that the patient has a satisfactory home, and work to go to. Even without this, early discharge may well be the best policy; after leucotomy one certified paranoid patient made repeated attempts to escape from hospital and though he was greatly improved and no longer driven distracted by his "tormentors", his escapes were countered by keeping him in a refractory ward. Ultimately he managed to escape and had not been readmitted during the next 6 months.

As regards the personality factors, rostral leucotomy is too limited an operation to have much effect on established personality traits. Sargant (1953) has repeatedly stressed that the more worried one is about doing a leucotomy because the personality remains good, the better will be the result. Ström-Olsen and Tow (1949) disagreed on the basis of their experience with standard leucotomy, but it is true of the present series that the better results have been in the more adequate personalities who have shown in the past a capacity for friendly relationships, adaptability, the capacity to work steadily, etc. Unfavourable features have been marked feelings of insecurity and passive dependent needs, secondary gain from illness, "necessary" symptoms, firmly established unsatisfactory behaviour patterns of whatever kind, and hysterical exploitation of illness. Greenblatt *et al.* (1953) from their study of schizophrenics conclude that "the greater the emotional maturity, the better the interpersonal relationships, the less personality disorganization and the higher the anxiety and tension, the better the outcome"; my conclusions from a study of markedly

different case material, are therefore similar. In any potential candidate for leucotomy we must ask:

(1) Would he be any better if his emotional tension were reduced, his depression lifted, his ruminative worry diminished?

(2) Has he personality "assets" which will enable him to reorganize his life to get some satisfaction for his needs.

(3) Is his environment satisfactory or can it be made sufficiently so?

(4) How extensive a lesion is likely to be needed and where should it be?

The answer to the last question is slowly becoming clearer; we now know that quite limited topectomies (Pool, 1951; Le Beau, 1953; Tow and Whitty, 1953), or cortical undercutting (Rylander, 1952; Scoville, 1954) may be adequate in patients with well preserved personalities. The results of rostral leucotomy confirm this; it is an adequate operation in most cases of affective disorder, and should certainly be considered in all other cases with well preserved personalities before submitting them to the often mutilating standard cut.

Summary

The results of rostral leucotomy in the first 240 cases operated on by Mr. Wylie McKissock are described. A personal follow up was carried out 1½ to 5 years after operation. The 3 rather different operative approaches, and the rating scales used in classifying the results are described.

There were 3 deaths attributable to the operation; only 1 death occurred in 177 consecutive blind rostral operations (0·6 per cent.); major non-fatal intracerebral haemorrhage in 1·7 per cent.; less severe bleeding in perhaps 5 per cent.; a frontal lobe abscess in 1 case. There is therefore an operative morbidity of about 7 per cent. but lastingly serious effects in only 1 per cent. Urinary incontinence in the early post-operative period occurred in less than 10 per cent. of cases and was rare after uncomplicated operation except where there were contributory causes. The morbidity is higher in hypertensive patients but not sufficiently high to make hypertension a serious risk.

Epilepsy occurred post-operatively in 4·6 per cent. of 196 cases whose operation was uncomplicated and who had no previous history of fits; in 24 per cent. of 21 cases after a second leucotomy; in 20 per cent. of 15 cases with probable undue operative haemorrhage, etc. Three patients had attacks of status epilepticus.

Six patients, 4 of whom were obsessional, were strikingly disinhibited during the early post-operative period; this condition appears to be distinct from post-operative attacks of hypomania observed in 10 cases of affective disorder of endogenous type, especially in recurrent depressive illness. Caution is advised in recommending this last type of patient for rostral leucotomy.

The Open O, Blind B and Blind G operations are compared. The open operation gives much inferior results and is no longer in use. There is little to choose between B and G, both of which give worthwhile results in two-thirds of the cases of affective disorder and psychoneuroses. There is a suggestion that intellectual deficits are likely to be more marked after G, and B is therefore recommended as the most satisfactory of the three operations. The therapeutic results are comparable to those obtained by standard or lower quadrant operations and in view of the slight personality deficits after rostral leucotomy it is suggested that this should replace the other operations in suitable types of case.

The importance of social, environmental factors is discussed. These may well determine the success or failure of the operation and should be carefully assessed in each case, with the idea that modifications may be brought about which will enable a patient to cope when his tension has been partially relieved by operation.

Success or failure depends largely upon three main factors:

(1) The extent to which symptoms, of whatever kind, depend upon distress, whether of tension, depression or ruminative thinking.

(2) The quality of the personality.

(3) The possibility of helping the patient to surmount environmental difficulties.

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PERSONALITY CHANGES AFTER ROSTRAL LEUCOTOMY: A COMPARISON WITH STANDARD PREFRONTAL LEUCOTOMY

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"STANDARD" leucotomy in the plane of the coronal suture is undoubtedly an effective treatment for many cases of otherwise hopeless prognosis. The main objection to its use, resulting in many "modified" operations being devised, has been the occurrence of serious personality deficits afterwards. Ström-Olsen and Tow (1949) found that these handicapped nearly three-quarters of patients with "severe neurotic depression, obsessive-compulsive neurosis and chronic tense hypochondriasis", and though 76 per cent. were relieved of illness only 8 per cent. were in full employment. Tow (1952) has repeated his concern at the serious damage inflicted on well-preserved personalities. Partridge (1950), who has given a full account of the personality changes after McKissock's (1943) "standard" leucotomy, detected some personality deficit in nearly every case of the 300 he investigated and suspected that intellectual impairment was present in all, though he could only be sure of it in a proportion. I have elsewhere (Pippard, 1955) reported the clinical results in 240 cases followed up $1\frac{1}{2}$ to 5 years after rostral leucotomy by Mr. McKissock and this paper should be consulted for details of the operative techniques and scales used for rating the results.

As recently as 1952 the writer of an annotation in the *Lancet* could say, of operations confined to the ventro-medial quadrants, "the cured patient is likely to be emotionally blunted and may become friendless".

It must be said at once that so far as rostral leucotomy is concerned this is unduly pessimistic, for it will be seen that in 95 per cent. of cases the personality changes are negligible. It seems worthwhile attempting a comparison with Partridge's series, of the effects of this operation on the personality; this will bring out the difference clearly.

Partridge considered in detail 60 patients who had recovered from affective disorders, since in these the changes directly due to leucotomy should be less obscured by persistence of changes due to illness. I shall consider the changes in 114 patients, selected, from those I followed up, by excluding any with schizophrenic or paranoid states, complicating organic nervous disease, dementia or known operative haemorrhage; those whose rostral operation was not their first; those still, or again, in hospital; those not personally interviewed or about whom, for some reason, there is insufficient information. In considering certain subjective changes I shall include 6 other patients also. Of the 114 cases, 21 had had Open rostral O operations, 70 Blind rostral B and 23 Blind rostral G.

Symptomatically, 21 had become free (rating S1), 53 were much improved (S2), 31 were improved (S3), and 4 were unchanged (S4). The result was good in 66, fair in 22 and poor in 26 cases.

Following Partridge's plan it is convenient to consider the changes under the headings of (1) activity, (2) affect, (3) restraint, (4) intellect.

(1) Activity

Thirty-nine of 114 patients still showed, at follow up, a post-operative reduction in energy or drive noticeable to their friends or to themselves which was referred to in such terms as "less drive"; "not enthusiastic"; "less of a go-getter"; "likes to take things easy"; "things are more of an effort for him"; "tire more easily".

A wife remarked, "He will sit now and read, or just sit; before, if you could get him to sit for 5 minutes it was a miracle. He doesn't want to go out; if there is no work to do all he wants is to go to bed. Sometimes I could scream." Another said that her husband needed more prodding. Eight patients spend more time in bed and a few take an unwonted nap, but none have had difficulty in getting up in the morning (a tendency to get up late persisted in 22 of Partridge's 60 cases at 2 years). The older patients were inclined, sometimes perhaps correctly, to attribute these slight changes to the passage of the years.

Five patients were slower at their work, and achieved less in the time, e.g. a middle aged housewife would still be doing chores at tea time which formerly were out of the way by lunch. Apart from reduction in energy, an intellectual deficit making it impossible to plan work as efficiently (particularly in 2 cases), partly accounted for their slowness.

Seven patients, in contrast to these, manifested an increase in activity and drive after operation, presumably because hampering symptoms had been relieved.

Lack of spontaneity was not a marked feature of these patients, in contrast to its comparative frequency after standard leucotomy; some patients may have been less spontaneous, but it was not enough for relatives to remark upon, and at interview was rarely found; one woman tended to be monosyllabic and another volunteered little except on questioning, but these patients are exceptional. It is exceptional, too, to find lack of persistence, the drifting from one job to another not more important, that was still noticeable in 28 of Partridge's 60 patients after 2 years; but of one man his wife said, "he never finishes a job: we haven't a clock or watch in the house that goes because he has them all in bits; before his operation I had only to ask for a thing for it to be done at once".

Reading: Questions about reading habits reveal deficits in the fields of activity, affect and intellect in about one-quarter of the cases. Many others, of course, have never been readers. No patient was disorientated and most showed a knowledge of current affairs (even if only of the activities of 'Jane' and 'Garth') consistent with their intelligence and education. Five patients certainly showed less interest in the news and three, though claiming to read several newspapers each day, showed remarkably poor grasp of affairs.

Questions about leisure occupations and reading were frequently met by apologies for not doing more, or by vague statements which on closer examination revealed a change in habits, e.g. an obsessional clerk professed an interest in the newspapers and books ("everything came back to normal within a few days of the operation") but in fact he rarely reads anything now but the *Reader's Digest* ("what with magazines and papers; you see you have lots of writing, and I get tired in the evenings; it is often more restful to sit and listen in; perhaps in the past I wouldn't have listened in so much"); others, too, are more ready to take their entertainment from Radio and Television but it is impossible to be sure that this is more marked in these patients than in the general population. Some find less interest in reading, or lack the drive to get books from libraries, finding it easier to skim through magazines which are

ready to hand; thus a man of 36 who read a good many detective stories before operation, now only reads when he casually picks up a thriller his mother has borrowed from the library: unless he finishes it at a sitting he doesn't bother to read to the end.

Nine patients found less time to sit and read, the commonest excuse put forward for not reading, but 2 patients relieved of their symptoms to a considerable extent, now read more, and 2 others have been able to relax and read for the first time in their lives. By contrast, a woman who would only relax with a book or her knitting now just relaxes.

(2) Affect

Deficits in this sphere were evident in 47 of the 114 patients, including 25 of those who also showed reduction in activity, and 4 of those who showed an increase. The most frequently noted changes were a tendency to be less concerned for others, more selfish, with diminished regard for appearances and the opinion of others (24 cases). Patients remarked of themselves, "I'm less sympathetic, harder", or "I'm an unfeeling little beast; when the child used to cry I would cry too, but now I will give her one . . ." Several patients had been unmoved by the death of loved relatives; the sister of one 66 year old who had been chronically depressed was deeply distressed at the patient's cheerful whistling round the house whilst her brother lay dying, and at her lack of concern when he died, "You would almost think she didn't feel things." The mother of a 34 year old obsessional postman said of his reaction to his father's death "he came through it wonderful; if he *was* upset he didn't let us know". A 65 year old hypochondriac, almost symptom-free, showed no distress when her only son emigrated a year after operation.

A young compulsive neurotic said, "I don't care what people think of me now", but resented it when her landlord "put upon" her. A deeply religious Scotswoman whose involutional melancholia had lasted 9 years said, "I can see now that people don't mean to hurt." One woman was described as "shrewder, drives a harder bargain".

Many patients obviously worried less, and this was referred to specifically in about a third of cases. "Nothing worries her now, she's always cheerful" was an observation repeated in various forms by many; 3 patients were euphoric, but only 1 of these was a little fatuous and giggly. Conscience obviously sat more lightly on several, e.g. 2 obsessional men who were more ready to take a few days off work for their own purposes than they had been in the past; one earnest young man summed himself up by saying, "sincerity has given way to expediency". Two other men are more ready to skimp things: the postman does not bother so much if he cannot deliver a letter! A few patients gave an impression of, and were themselves conscious of, a loss of affective depth; 2 hysterical psychopaths both regretted the felt loss of capacity for great joy, the price they paid for a reduction in the downswings of despair, and one found that Tchaikowsky's music had lost its power to move her, though she could still appreciate the more primitive rhythm of Ravel's "Bolero", and was more interested in dance rhythms generally than she had been. An anxious obsessional also lost some of his capacity for musical pleasure. By contrast, another obsessional patient became appreciative of music only after his successful leucotomy, but much of his appreciation is that felt by one craftsman for another and seems to be in good measure intellectual.

A tendency to be less concerned with past events, implicit in the present contentment of many, was made explicit in 2 cases: "I can talk about the past

without any feeling", said one, and another talked of harrowing experiences without the slightest distress, and her daughter said that she had become less "shockable". A lessened concern for the future was also evident in several patients; 3 were not as careful with money: a husband said, "she used to be careful, preparing for the future; now it seems to be spending for the day", but in only one case was a carefree frittering away of money on his personal comfort and pleasure a source of real anxiety to his wife.

A number of examples have been quoted to show the sort of changes which have taken place but it must be emphasized that though about one-third of the patients show a noticeable reduction in activity and energy at follow up, and about one-half have recognizable affective deficits, yet in comparatively few is there anything to upset either patient or relatives.

Tearfulness: crying was, of course, a frequent expression of misery in these patients and it was only to be expected that with the relief of depression and anxiety there would be much less.

This was so, but what was unexpected was a complaint made by a patient early in my investigations that she could no longer cry even when she wanted to. Further questioning revealed 9 patients who had found themselves unable to cry since leucotomy and 8 of them regretted it (there were of course many others who don't cry but feel no desire to); "If you get upset about something, having a cry lets it out. Yes, I try to cry but it doesn't come, and I used to be very tearful." Only 2 related the loss to being "harder" or to feeling that things no longer affected them; the others definitely missed having a "safety valve" to release pent up feelings.

Two other patients noticed an increase in involuntary tearfulness; a man who finds himself weeping at the cinema much more readily, and the Scots-woman already mentioned who finds that tears only come in association with laughter, which itself comes perhaps too readily.

Freeman and Watts (1942, p. 290) quote, in a letter from a patient, "several years ago I could weep and relax when things piled up too high for me emotionally. I'm not able to weep any more and I take my spells out in talking too much."

The "visceromotor apraxia" evident here suggests that part of the relief of anxiety and tension by leucotomy may be due to a reduction of the somatic manifestations of emotions, perhaps by a direct interference with fronto-hypothalamic pathways. A relief of somatic anxiety was the only noticeable effect of leucotomy in one routine-bound obsessional whose symptoms had maternal approval.

(3) Restraint

Personality changes under this heading were noted at follow up in 52 of 114 patients. The change most commonly mentioned by relatives and very often by the patients was increased irritability, a tendency to flare up more quickly though almost always the anger was short lived and afterwards they bore no grudge, sometimes a welcome change. This "touchiness" was shown by 26 patients. It had certainly been present earlier in several who were no longer touchy and probably others had forgotten about it. By contrast, 11 patients were reported better in temper. One of these and 12 of the more irritable patients were less restrained in speech with an increased tendency to speak what was in their minds; another 20 patients were more outspoken but without any apparent change in temper.

In 5 patients only did the outspokenness amount to anything like tactless-

ness. Tactlessness involves, in addition to lack of restraint, a reduction in empathy and in the capacity to appreciate intellectually what the situation requires; when one man, after standard leucotomy, held a long conversation with his sister-in-law about the recent death of her child, it seemed that his tactlessness arose not only because he was less restrained but because he could no longer imaginatively enter into her experience, and saw the situation only as one calling for conversation. His wife said of another, "he has lost his kindliness in pointing out things gently". One woman, never on good terms with her husband, spoke her opinion of him openly in the street where previously she had confined her confidences to her teaparties. For the most part outspokenness was unimportant and in several cases was welcomed, husbands approving of the way their wives could give as good as they got in verbal exchanges with neighbours or tradespeople. It was sometimes a nuisance though, as when a butcher was antagonized, at a time when meat was scarce, by expressed doubts about his honesty as a tradesman.

A young woman, aggressive and impulsive anyway, went to a Labour Party meeting during the General Election some months after her rostral leucotomy. The chairman introduced the candidate for re-election with the words "I am sure you will all agree with me that we have never had a better M.P. than ——", whereupon the patient said in a loud voice, "What about Winston Churchill" and had to be removed shrieking from the meeting when the staunch supporters of the candidate turned on her. This outspokenness surprised her husband and the neighbours but was negligible by comparison with the lack of restraint she showed later, after standard leucotomy, when, clad only in her nightdress, she chased her young son round the garden shrieking murderous threats at him.

No relative of any rostral leucotomy patient had any reason, like the husband of a patient after her second, standard, leucotomy, to be on tenterhooks whenever they went out socially for fear of what innocent but tactless remark might next fall from her lips.

Diminished restraint was evident in other ways in a few patients; one woman, rendered less sensitive and more superficial, was less reserved and got more fun from her life. Three patients were noticeably more demonstrative of affection to their spouses. Only one patient did anything to bring her into conflict with the police, but was not prosecuted: she stole a few spoons as an act of petty revenge; this was in keeping with her immature, hysterical personality, but she had not previously acted in this way; her impulsive second marriage soon after operation may also be regarded as in part due to lack of restraint, as well as in part to a lack of judgment.

In considering the importance or otherwise of the changes in personality noted, we must never lose sight of the personality setting, nor of the circumstances which call forth the manifestations. As Partridge demonstrated, the changes are not always present but may be regarded as tendencies concealed or revealed according to the demands of the situation. Thus, after 7 years in hospital, a man came home to his wife who had a life of her own; with her he was rudely outspoken and critical, and within 3 months she left him. With everyone else, and at his work which he does well, he behaves normally and shows no lack of restraint.

(4) Intellectual Changes

Fifty-eight of the 114 patients were considered to show evidence of impaired function intellectually. In addition I shall consider 6 other

patients who were excluded because there was nobody to give information about other personality changes, but who themselves supply the necessary information about their intellectual functioning: 3 are impaired.

Patients usually mentioned difficulties spontaneously; if they did not do so it was unusual to elicit them by questioning. There were 2 main types:

(i) memory difficulties;

(ii) difficulties with conceptual thinking.

(i) *Memory Difficulties*

(a) *A forgetting of whole sequences of past experience*, always in a patchy sort of way: 16 cases. In some the memory could be recovered by a suitable reminder, e.g. a patient had forgotten the withdrawal of the B.E.F. from Dunkirk until reminded of it by reading Churchill's *War Memoirs*, but another could not recall Dunkirk even when reminded, and in other cases too the episodes seemed permanently lost.

In the group of 120 patients 64 had had more than 6 E.C.T. in the past and 13 of these (20 per cent.) reported "lacunar" memory deficits. Fifty-six had had less than 6 E.C.T. and only 3 of these (5 per cent.) had deficits.

(b) *Difficulties with retention and recall:* 38 cases. In contrast to the lacunar memory defects which always involved pre-operative experiences, these are present troubles. I have excluded a few patients who complained of memory troubles before as well as after operation.

As examples, many patients find themselves more absent minded; they put things down and lose them (5 cases), they forget things whilst shopping which they had intended to bring in (4 cases), they find it necessary to make lists, memoranda, etc. (3 cases). One said he could not sustain thought and had to jot down at once what occurred to him, and another said "I don't remember things I'm told even when I'm interested and have taken them in". Two young women, resuming nursing, found themselves much slower at learning than they had been, with difficulty in taking things in and a need to repeat things to themselves over and over again. One woman was slow in learning a new job because she forgot what she was told, though she recognized it when told again.

Many patients found it more difficult to recall names or to fit names to well known faces, and one overcame this by deliberately associating something else with whatever name he wanted to remember, e.g. Brown with Paper. It seemed that there was an exaggeration in these people of the well known phenomenon of "having something on the tip of one's tongue", and often the required name or information would pop into the mind later, sometimes much later, showing that it was somewhere all the time but not available; a wife said, "he will forget things you have told him within the hour and then perhaps remember it a day or two later"; a photographer who had had, as he said, a "photographic memory", could no longer connect people's faces with photographs of them he had taken in the past; a husband said, "she has an excellent memory if things are recalled to her but she cannot recall them spontaneously as easily as she used to do". The woman who could not recall Dunkirk said, "I can remember things as you talk about them but I can't go back on them and call them to mind . . . if I am going to make a pie I don't know how to start, and to be truthful I guess it and it always comes out all right." Examples such as these could be multiplied but enough have been given to indicate the sort of associative memory difficulty observed in 5/21 O, 24/73 B and 11/26 G cases; though a source of minor irritation to the patient, it rarely seems of practical importance.

(ii) *Disturbances of Conceptual Thinking*

Disturbances of conceptual thinking were noticed in 26 of 120 patients; 12 of them had difficulties with retention and recall also.

(*a*) Loss of ability to plan work was found by 6 patients; a skilled dressmaker found herself making elementary mistakes such as cutting out a centre-back to a selvedge, and gave up this work to become an invoice clerk; a painter finds that having finished painting a room he may have omitted to paint a large patch on one wall; a previously efficient housewife was less able to plan a meal for more than the usual number and tended to overstock the larder. Inability to carry through a job to completion, as in the case of the man who had all the clocks in pieces, may show a lessened capacity to plan; certainly at his work as a builder he is much less efficient than he once was. There seemed to be a similar intellectually determined inefficiency about their housework in 2 others.

(*b*) A lessened capacity to deal with more than one thing at a time; 5 cases, including 3 of those just considered; the dressmaker, for example, found it necessary, where it had not been so before, to give undivided attention to boiling milk or making toast. If she tried both together, the milk boiled over and the toast burned.

(*c*) Four patients experienced greater difficulty in comprehending what they read or heard. An accountant could not understand what he read in technical books at a standard he could previously tackle.

(*d*) Three patients complained they could not do crossword puzzles so well, but this is too complex an intellectual exercise to analyse in detail; associative memory impairment may be one of the factors involved.

(*e*) Eight patients seemed to have a difficulty in calculating not present before. Since a minority of patients had been adequately tested in this respect before operation objective evidence is lacking but 2 patients could reverse only 5 instead of 7 digits at follow up and the latter, a business man, could not work out discount correctly. An hotel book-keeper, long accustomed to such exercises before operation, had found herself, to her surprise, unable to work out $2\frac{1}{2}$ per cent. of £2,000 and when given pencil and paper showed no idea of even the first principles. One young psychopath showed an interesting failure initially in taking 7 from 100, despite a willingness to co-operate, but did the serial subtraction correctly in 55 seconds once he had grasped it: "100—7? equals 103 wouldn't it? No, Christ no, 113. No, 199, 198, no it *can't* be 190 something . . . 7 from 10 is 3; it can't be 113. It's 90 something, 93!" (triumphantly).

It is important to note that such difficulties are unusual. I made a habit of asking patients to repeat digits forwards and in reverse, to take 7 serially from 100 and to attempt simple arithmetical calculations, whether such tests had been recorded before operation or not. These cases are the only ones in the total 120 where the performance differed significantly from any previously recorded or from what might reasonably have been expected from a person of that intelligence and education. Partridge found that 26 of 35 patients showed a reduced ability to reverse digits.

(*f*) Five patients referred in such general terms to their intellectual deficits as "mind slower", "less intelligent", "less alert".

(*g*) Several found a difficulty in concentrating which had not been present before operation. This is a complex function and was disturbed for different reasons; 2 patients could not maintain a train of thought, and in one this was clearly related to his difficulty in retention; perhaps it is a similar disturbance of function which makes concentration effortful instead of automatic for another

and which makes reading a book too much of a strain for an elderly woman. In these cases one has the impression that their capacity for sustained attention is reduced, a deficit which may underlie intellectual difficulties classified under other headings, e.g. difficulty in comprehension. Certainly in one case, and probably in others as well, the affective factor of lack of interest seemed more important than a specifically intellectual deficit in determining lack of concentration.

(*h*) One 35 year old schoolteacher blamed the leucotomy for complete loss of visual imagery similar to that discussed in 2 cases by Brain (1954). Other intellectual impairment was evident in her inability to give an ordered history and in a marked impairment of associative memory; she could reverse only 4 digits. Geographical remoteness made further investigation of her case impossible, but 14 months after operation she had had a severe attack of status epilepticus and though there was no evidence at the time of any operative complication this obviously cannot be excluded; in this case, as in Brain's, there is not enough evidence to allow localization of the responsible lesion.

Difficulties in conceptual thinking were observed in 0/21 O patients, 18/71 B patients and 8/26 G patients. It is possible that in the longer follow-up period of the O cases deficits present at an earlier stage may have diminished but my impression is that the deficit is more marked in the G cases than in the rest, in 3 of whom there are grounds for believing that the operation was unduly extended by operative haemorrhage. It is more likely that the greater damage of the more posterior G incision is the real explanation of the difference.

Discussion of the Intellectual Deficits

Many patients blamed the leucotomy for their intellectual deficits and one was unusually definite: "E.C.T. affected my memory so that I could not believe I had had it, but if people speak to me I often have to ask them their names . . . that is how the operation has affected me." Several patients asserted that their memory disturbances dated from E.C.T. given before operation. It is generally accepted that the memory disturbances caused by E.C.T. vary with the amount given and usually disappear within a few weeks or months (Lowinger *et al.*, 1946). Zubin (1948) found that recall and relearning show complete loss after shock but that recognition is hardly touched, and learning and retention return to at least as good as before within about 3 weeks. Michael (1954), using Rylander's noun enumeration test, found a significant decrease in scores after 5 E.C.T. with return to normal within a week of stopping treatment. Janis (1950) describes a patchy amnesia after E.C.T. and guardedly concludes that there is "some kind of interference with the normal production of habitual verbal associations", such as I have recorded in these patients; he mentions some memory losses persisting for more than a year. Sargant and Slater (1954, p. 96) state that a "slight degree of impairment, in most cases temporary, does exist in the majority of patients shortly after the conclusion of a course of treatment . . . in exceptional cases it may persist for very long periods or indefinitely"; they comment on the inadvisability of giving prolonged courses of E.C.T. because of the effect on memory.

It is one thing to suspect that the impairment of memory complained of after leucotomy may be partly due to electroplexy, even though patients themselves may attribute it to the operation; it is quite another matter to demonstrate it convincingly. For example 25 of the 37 patients (68 per cent.) with difficulties of retention and recall had had more than 6 E.C.T. before leucotomy, and 9 of them more than 24 E.C.T. Of 54 patients with no detected intellectual deficits

of any sort 22 (41 per cent.) had had more than 6 E.C.T. and only 1 more than 24 E.C.T. Statistical analysis of the figures is not justified since the group with no detected intellectual deficits is not a true control group; it may be that the experience of E.C.T. amnesia in the past predisposes to awareness of memory disturbances after leucotomy, so that on these grounds alone the group reporting memory disturbance must be regarded as suspect, since it is largely self-selected. The fact that the two groups do not differ from each other in any striking way, e.g. diagnostic categories, level of intelligence, does not overcome the objection; if one excludes the O cases, who had comparatively fewer E.C.T., a less extensive operation and a longer follow up period, and the G cases, who had more E.C.T., more extensive operation and shorter follow up period, leaving only the B cases, which form a more homogenous group, we find that 3 of 21 with less than 6 E.C.T. have deficits in retention and recall compared with 16 of 31 with more than 6 E.C.T. Though the difference is heightened the groups are still not properly comparable.

The type of memory disturbance under consideration, an impairment of association, is well recognized after more extensive operations and it is of interest that 5 of 8 G patients who had less than 6 E.C.T. show such a deficit and 6 of 9 who had more than 6 E.C.T.

Though nothing is proved I am left with a clinical impression that E.C.T. given before leucotomy may increase the amount of memory impairment noticed after leucotomy, though anything attributable to electroplexy may be swamped with a more extensive cut than B.

Conceptual thinking difficulties are of a type not seen after electroplexy and are reported in this series independently of the amount of E.C.T., but, as already mentioned, tend to be more severe after G than after the other operations.

Whatever the basis for the increased reports of memory disturbance by leucotomized patients who have had much E.C.T. there are clinical grounds for repeating Sargant and Slater's warning, quoted above, against giving long courses of E.C.T. In 2 cases given 76 and 152 treatments the severe memory impairment might have been avoided by earlier operation, which successfully relieved symptoms in both.

(5) Work Adjustment

There is a dearth of professional occupations in this series (the only professional man, a chemist, had been keeping house for years whilst his wife went out to work); there is no indication amongst these cases that the type of occupation makes any difference to the work adjustment after leucotomy.

As might be expected, those who are relieved of their symptoms achieve a better work adjustment than those who are not. Table I shows the relationship between work ratings and ratings for symptom relief.

Forty-five of the 114 patients were working as well as ever in their lives, and 32 more at a very satisfactory level considering the degree of incapacity they had suffered through illness. The work adjustment can thus be regarded as good in two-thirds of these cases.

Only those call for special comment who despite considerable symptom relief fail to achieve a good work adjustment, the 9 cases shown in the right upper quadrant of Table I. In 4 cases the personality deficits, though not severe, were such as to make these never very sound personalities less effective than the symptomatic relief might lead one to expect. One lost her job as a waitress because she was too abrupt with the customers, and another lived in a constant

TABLE I

	W.1 (Up to best previous level or better)	W.2 (Much improved but less skilled or lighter than best previous)	W.3 (Working but efficiency still impaired)	W.4 (No change)	W.5 (Worse)
S.1	12	6	3	0	0
S.2	28	19	5	1	0
S.3	5	7	4	14	1
S.4	0	0	0	9	0

i.e. of 21 rated S.1. 18 (86 per cent.) rate W.1 or 2.
of 53 rated S.2. 47 (89 per cent.) rate W.1 or 2.
of 31 rated S.3. 12 (39 per cent.) rate W.1 or 2.
of 9 rated S.4. 0 (0 per cent.) rate W.1 or 2.

stew because of her worsening relationship with her brother, to which her increased shrewishness contributed. She and another patient showed an increased distractibility which made them less efficient housewives.

In 4 cases life circumstances had altered so that much less was expected of them; a lonely widow had nobody to encourage her to be more effective, and little incentive. Their daughters had taken over most of the work from 2 cases, to the ineffectiveness of one of whom a rather fatuous euphoria contributed. She was an elderly hypertensive and is thought to have suffered more damage than intended. The retirement of one man from even a nominal connection with work was in part hysterically motivated.

There is insufficient evidence to show whether rostral leucotomy does or does not produce such personality deficits as might interfere with highly skilled and responsible work; however a business man who had to live by his wits was hampered by impairment of associative memory and of ability to do mental arithmetic, as well as by the diminished drive and slightly lessened sense of responsibility and impaired business acumen which persisted after a phase of post-operative hypomania had subsided.

No patient could be called a creative worker, but there were several skilled craftsmen (notably 2 toolmakers and a cabinet maker) who retained their skills.

(6) Religion

Despite special enquiries the results are meagre. The great majority of patients have never given more than lip service to religion, and few even as much as that. Those who were churchgoers before operation usually continued afterwards though some were more lax. One goes "more when I feel like it" than she did and another is "not *quite* so regular".

Apart from external observances an R.C. convert has found religion even more important and "more real" since operation; along with this goes an acceptance of the unfulfilment of her ambitions, and finding "the Great Unknown less towering".

A depersonalized obsessional is "less concerned about the ultimate things".

Another obsessional has found a deepening of his personal religion as a result of freedom from neurotic fears and yet another finds her prayers clear now, undisturbed by obsessive thinking.

A middle aged spinster, disgruntled as always, maintains her trust in the future life because the present is so unsatisfactory and resents that others are slack in attending church.

One of the skilled craftsmen still enjoys phantasies of being a very religious person.

The Scotswoman, already quoted, expressed the view that her illness had its place in the Divine purpose for her. "I feel I have been reborn into a new world and can see that all the experience of those 8 years is very important to me . . ." Her faith has been deepened as a result and she feels that it is securely hers now and not merely her father's.

An Anglican clergyman found no change in his devotional life.

The only conclusion one can draw is the very general one that the religious attitude is not directly affected by rostral leucotomy but is liable to be affected in the reintegration of the personality after operation, as indeed it may be in the reintegration after psychotherapy or any other treatment. This agrees generally with the experience of Sargant and Slater (1954, p. 269) after modified operations.

(7) Sexual Adjustment

There were minimal changes in the sexual adjustment of these patients. Where loss of interest was symptomatic, e.g. of a depressive illness, recovery from illness was usually accompanied by a return of sexual interest. Where frigidity was symptomatic of a personality disorder it was rarely affected, though one hysteric seemed a little less frigid and two obsessional women permitted sexual intercourse where previously they had refused their husbands because of obsessive guilt. Another allowed more frequent intercourse and derived occasional pleasure but "my husband knows what is good for him and has never worried me". One young woman has married happily and had a baby since leucotomy.

An obsessional man found that sexual intercourse left him physically exhausted for only 24 instead of 48 hours! A young psychopathic rag and bone man became actively homosexual for the first time 2 months after leucotomy but he had been associating with homosexuals for a long time and it was probably a question of when? rather than whether? One man, otherwise unchanged by operation, was impotent for 3 months and has since suffered from premature ejaculation; it is likely that this is psychogenic.

Summing up, there is little change in sexual adjustment except in so far as lessening of restraint and freedom from anxious guilt permits more freedom in intercourse.

(8)

Table II

Compares the Ratings for Symptomatic Relief (S) with the Ratings for Personality Deficits (P) After Rostral Leucotomy

	P.1 (On balance resulting in improvement)	P.2 (None, or indefinite)	P.3 (Slight)	P.4 (Marked)	Total
S.1	6	3	10	2	21
S.2	6	12	30	5	53
S.3	1	14	14	2	31
S.4	0	7	2	0	9
Total	13	36	56	9	114

i.e. with symptom improvement rated 1 there is some personality change in 18/21 (86 per cent.)
with symptom improvement rated 2 there is some personality change in 41/63 (77 per cent.)
with symptom improvement rated 3 there is some personality change in 17/31 (55 per cent.)
with symptom improvement rated 4 there is some personality change in 2/9 (22 per cent.)
($\chi^2 = 13 \cdot 10$, n = 2, $p = < \cdot 01$)

6 of 18 (33 per cent.) rated S.1 were regarded as changed for the better and 6 of 41 (15 per cent.) rated S.2. and 1 of 17 (6 per cent.) rated S.3.

This suggests that, when symptoms are relieved, personality deficits may be acceptable and regarded as good which in a setting of continued illness might have proved irksome; for example, outspokenness in a happy person may be an attractive trait but not in a disgruntled and miserable one.

Frankl and Mayer-Gross (1947) considered that symptomatic relief depended on producing a counteracting degree of frontal lobe deficit symptoms. Meyer and Beck (1954) related symptom relief to an "adequate" cut (which would incidentally bring about more personality changes than an "inadequate" one).

The figures for the rostral series at least indicate that symptomatic improvement and personality changes are related, and it seems likely that both are dependent upon the extent of the cut.

The rating P.4 was given to only 9 of the 114 patients and it is useful to enquire why there should have been this degree of personality change, common enough in patients after standard leucotomy. The explanation which suggests itself is that post-operative bleeding may have increased the amount of damage to something like that deliberately produced by standard leucotomy. In favour of this is that 4 of these patients are amongst the 13 in the series of 114 who were incontinent during the first few weeks after leucotomy; one of these was doubly incontinent and he and another patient also showed more inertia and confusion than is usual after rostral leucotomy. Two of the 13 incontinent patients were only incontinent once, one had been incontinent before operation, and one, who was rated P.1, showed marked personality changes which would have justified rating P.4 had they not been desirable.

Thus 4 of 10 patients with marked personality changes were amongst those 10 in the total 114 who are suspected on other grounds as well of having had a more extensive lesion than usual. These figures support the hypothesis. In 2 other cases epilepsy since operation may well be related to the personality changes.

(9) Personality Changes in Cases Later Submitted to Standard Leucotomy

Thirteen cases, including 3 who had unilateral operations, satisfy the criteria laid down for selecting rostral patients for consideration of personality changes; in the one unilateral case symptomatically much improved the decreased restraint and diminished sensitivity make her a more satisfactory personality than before. There was some evidence of intellectual deficit, notably a difficulty in spelling not present before, which she says is because she can either see the word in her mind's eye or try to spell it but not both simultaneously. She can, however, write the word down correctly, and it is only a few words which have caught her out in this way. She constructs her sentences inaccurately at times, e.g. "When you get it up I will straighten it down" instead of "When you get up (from your chair) I will straighten it.". Two dullards in the rostral series and one other complained of a similar spelling difficulty. Another unilateral case was not helped by the standard leucotomy, and an intellectual difficulty appeared which was not present before: she found herself unable to deal with propositions in the form Either . . . Or . . . The enunciation of the second alternative erased from her mind the memory of the first and she could not compare the two in order to reach a decision. No rostral patient had an intellectual difficulty quite like this.

The third unilateral case also noticed intellectual difficulties after the standard operation, particularly that his "powers of recall have been inter-

fered with" (comparable with many patients in the rostral series) and also that he no longer just knows what day it is but has to work it out by deliberate "piecing of it together".

Of the 10 patients who had a bilateral standard leucotomy 1 is rated P.2 (an involutional melancholic who seemed unaltered by either of her operations); 2 are rated P.3; 6 are rated P.4; 1 is rated P.5.

The personality changes in the 7 patients rated P.4 or 5 are more severe than in any patient in the rostral series. In one they do indeed amount to virtual destruction of the personality and Dr. Partridge tells me that this is the worst result of leucotomy in his experience. Another case, excluded because she was in a mental hospital at follow up, is very similar.

(10)

In order to compare the effects of leucotomy on the personality it is convenient to arrange the cases in groups more or less corresponding to Partridge's (Table III); from this it is at once evident that the changes after rostral leucotomy are usually of little consequence, being negligible in all but about 5 per cent. of cases symptomatically much improved, compared with 56 per cent. of cases after standard leucotomy.

TABLE III

Comparison of Personality Changes after Rostral and Standard Leucotomy

	Partridge (1950) (59 cases) Per cent.	Rostral (*a*) All (114 cases) Per cent.	Rostral (*b*) S.1 & 2 (74 cases) Per cent.	Standard after Rostral
1. Virtually no personality change or changes so slight as to make no significant difference	16 (27)	50 (44)	28 (38)	1
2. Slight changes present but making no important difference in their lives	10 (17)	56 (49)	42 (57)	1
3. More marked changes so that families are constantly aware ..	12 (20)	3 (2·5)	2 (2·5)	3
4. Patients difficult to live with but less so than ever before	4 (7)	3 (2·5)	2 (2·5)	–
5. Positively undesirable changes ..	17 (29)	2 (2)	—	5

N.B.—This table was prepared independently from Table II since Partridge's categories are not quite equivalent to the personality ratings I have used.

The figures for the rostral series are given in 2 columns (*a*) the whole group of 114 patients; (*b*) those with symptoms much improved, or symptom free (and therefore more comparable with Partridge's).

SUMMARY

The effect of rostral leucotomy on personality in a selected group of 120 non-psychotic patients followed up at home 1½ to 5 years after operation is described and compared with the effect of standard leucotomy in Partridge's (1950) series.

One-third of patients still showed a noticeable reduction in "drive", but a few had been more active since operation than they had ever been. Few patients showed much reduction in spontaneity, but there was a tendency for leisure pursuits to be less active.

Nearly half the patients had detectable affective deficit; particularly, they tended to be less concerned for others, more selfish, less sympathetic. They worried less and were more contented. However, the changes were rarely more than slight and in comparatively few was there anything to distress either patient or relatives.

Nearly half the patients were less restrained; this showed chiefly in speech and temper; tactlessness was exceptional and never a problem, indeed the freedom of speech was often welcomed by relatives. The quickly flaring but rapidly subsiding temper was readily accepted by families, who often preferred it to the sulks and grudge-bearing of the past.

Half the patients had some intellectual impairment, but rarely of more than academic interest. Patchy amnesias and defective retention and recall were frequent and have been noticed more by patients who in the past had more than 6 E.C.T. Disturbances of conceptual thinking, present in about a quarter of cases, seem to have no relation to E.C.T., but are a little more marked in G cases than in B, and were not observed in O cases.

There were no active professional people in the series and therefore there is no evidence about the effect of rostral leucotomy in highly skilled and responsible workers. The work adjustment after operation ran closely parallel to the symptomatic relief; it was unusual for any lowering in status at work to be due to the effects of leucotomy. Sixty-seven per cent. of patients were in full employment or keeping house as efficiently as before illness.

Religious attitudes are not directly affected by rostral leucotomy.

There is little change in sexual adjustment except as a result of relief of illness.

Ratings for personality changes are significantly correlated with ratings for symptomatic relief. Both are considered to be related to the extent of the leucotomy lesion.

Personality deficits were more marked in 10 patients (9 per cent.). There is some evidence that where changes are marked the operative lesion has been more extensive than it should be, either because it was misplaced or because of post-operative haemorrhage or venous thrombosis; in 2 cases the marked personality changes may be related to post-operative epilepsy.

All but one of 13 other patients who later had unilateral or bilateral standard leucotomy suffered an increased personality deficit and in 7 cases the losses were more severe than in any case in the rostral series.

Personality deficits are negligible after 95 per cent. of rostral leucotomies which have given good symptomatic relief, compared with only 44 per cent. of standard leucotomies. Positively undesirable changes were present in only 2 of 114 cases, compared with 29 per cent. of standard leucotomies.

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SECOND LEUCOTOMIES

By

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BILATERAL blind rostral leucotomy has been shown to be an adequate operation for the relief of many tense psychoneurotic and depressive states (McKissock, 1951; Pippard, 1955); the operation gave worthwhile results in about two-thirds of such cases in a series which included many who were unsuitable. This paper is concerned with the results in 27 cases operated on more than once.

Four patients had already had standard leucotomies with inadequate relief of symptoms; an open rostral leucotomy in one of these, a young ruminative schizophrenic, made no obvious difference. Another schizophrenic had a rostral G leucotomy to divide fibres in the inferior medial quadrant which might have been missed by the earlier standard operation (Sargant, 1953). Afterwards she no longer needed maintenance E.C.T. to keep her at a good level; reduction in tension which followed this limited incision, and the greater ease with which she could be cared for in hospital certainly suggests that a limited operation on the medial side may well be considered in some cases in which standard leucotomy has failed, and certainly before undertaking anything as drastic as Freeman and Watts' (1950) radical operation.

Another patient similarly submitted to a rostral G leucotomy had slowly relapsed after an initially successful standard leucotomy for a chronic tension state. He had, however, been left with a marked intellectual deficit and troublesome urgency of micturition and, if anything, his deficits were increased after the second leucotomy, without any useful relief of symptoms.

One man who had had several prolonged depressive illnesses which finally did not respond to E.C.T. was not relieved by an asymmetrical anterior standard operation, limited, on one side, to the inferior quadrant; 4 months later he recovered without obvious deficit, after a rostral B leucotomy.

Twenty-three patients who derived no help from rostral leucotomy, or whose symptomatic relief was insufficient or merely temporary, had a second leucotomy, rostral G in 1, unilateral standard in 3 and bilateral standard in 19.

An aggressive and bossy young woman, with the manners of a rude schoolboy, a compulsive worker who so feared being alone with her thoughts that she continued working through most of every night, was little changed by a rostral B operation but became postoperatively epileptic. More than a year later a rostral G leucotomy was done which was complicated by delayed recovery of consciousness, presumably due to some intracerebral haemorrhage. Besides slight personality changes, only evident to those who knew her well, the only sign of any alteration was that she needed rather less heavy sedation afterwards; she was still in hospital a year later.

In the unilateral standard cases environmental factors seemed to be of considerable importance in deciding success or failure.

A 28 year old woman, the less favoured of 2 sisters, formed clinging attachments to various people from puberty onwards. At 23, distress and depression, with homosexual ruminations and associated feelings of unreality, was treated unsuccessfully with modified insulin and E.C.T. and later by 3 years of psychoanalysis; this eased her guilt somewhat but encouraged the spread of ruminative thought. Open rostral leucotomy in 2 stages made little

difference but she was somewhat less tense and with much supportive psychotherapy, giving partial satisfaction of her dependent needs, was able to work on and off, for periods of a few months. Four years later a left standard leucotomy made no noticeable difference except that the resulting intellectual deficits were another source of anxiety. She spent most of the next year in hospital, but then achieved another dependent relationship, this time to a dianeticist, was temporarily freed of depersonalization for the first time in 10 years, and again started work.

Another young woman, the tenth child of a neurotic father who took little interest in his children, was always shy, timid and anxious, with few interests and no friends but her mother. She was liable to depressive mood swings and to obsessional rumination. She married at 20 and they lived unhappily with her parents, where gradually she grew more tense and obsessional, taking hours over the simplest job and requiring constant reassurance, e.g. that she had had her breakfast. She spent a year in a psychiatric hospital, but soon relapsed and a year later had a blind rostral leucotomy. For 2 months she was better but began to relapse as soon as she returned to her parents' home. A suicidal attempt 18 months later was the occasion for left unilateral standard leucotomy, following which she left hospital to go to a new home with her husband, away from the family tensions which had proved too much for her. Eight months later she had gained weight, was more relaxed and no longer bit her nails, a sign of tension she had had since childhood. Her husband thought that there were no unpleasant personality deficits, and that her carefree attitude made her better than she had ever been. She remains fundamentally inadequate, obsessionally rigid and phobic, but is troubled by none of the distressing tension, ruminations or depersonalization for which operation was done. Intellectual deficits, obvious at interview, are of no importance in her life. The move away from the parents' home may well have determined the success of this leucotomy just as the return to the stressful situation may have prevented the rostral operation from having more than a temporary effect.

Nine months after initially successful rostral B leucotomy, a 36 year old homosexual clerk, who from puberty had struggled against compulsive rechecking and elaborate toilet rituals, relapsed after being given too much responsibility in a hospital where he worked as a ward orderly. Left unilateral standard leucotomy only added to his burdens a slowness of thinking and memory difficulties. In his case the difficult problems of resettling him in work and providing a measure of security were not solved, so that resentment and feelings of hopelessness were intensified during the next three years. He then got suitable work as an hotel porter and when last heard of was no longer disgruntled, and apparently little handicapped by his obsessionality.

These three cases illustrate the importance of adjusting the social environment to the post-operative capacity of these inadequate and dependent personalities. Unless there is some prospect of doing this there seems little point in trying to adjust them by progressively more extensive leucotomy.

Bilateral standard leucotomy as a second operation gave poor results in 10 cases, frankly disastrous results in 2, fair results in 4 and good results in only 3.

Amongst the 10 poor results are 9 in which it is not unexpected; 2 had become chronically manic after rostral leucotomy and though the second operation damped down the manifestations of mania the mood remained unchanged and personality deterioration was severe. Of 4 schizophrenics, 3 were of simple or hebephrenic type carrying a poor prognosis, and one was a dangerously hostile paranoid schizophrenic, whose illness was virtually unaltered by either operation. The failure in one case of involutional melancholia in a deaf little woman with tinnitus is not perhaps surprising:

She lost her home in an air-raid and had to live in an uncongenial neighbourhood away from the friends of former years, her family had grown up and left her, and her personal contacts were limited to a few cronies in the local pub.; only there did she brighten up at all. There were no obvious post-operative personality deficits and her unobservant husband had not seen any change in her.

One hopelessly inadequate psychopath was relieved by standard leucotomy of his obsessional symptoms but continued residence in a mental hospital was needed because, not surprisingly, he had lost most of what little initiative he had ever had.

One young woman had a rostral B leucotomy for the 4 year depressive illness with many hysterical features which followed the birth of her only child. Her marriage was unhappy and she had killed the baby. The first operation had little effect, but for 10 months after standard leucotomy she was much more energetic. Then followed a prolonged depressive illness during which she made a determined suicidal attempt, and later 4 months of hypomania during which, for the first time, she came to resemble the typical "frontal-lobe" patient, with her gay, carefree living for the moment, extravagant spending, outspoken rudeness to her husband, etc. Once more she slumped into depression and it seems that this is really a case of manic-depressive psychosis. As is well known, even extensive leucotomy may not prevent the recurrent mood swings of affective psychoses.

So far, then, there is no reason to be surprised at the failures.

An obsessional Civil Servant of 56 was utterly demoralized and incapacitated for 2 years by pain after ophthalmic herpes zoster. Open rostral leucotomy gave some relief for less than a week, and then he was less controlled in his complaints and appeared to suffer even more. Five months later standard leucotomy reduced him to a sarcastic person with marked frontal lobe deficits. Nearly 3 years afterwards he had managed to continue his work, but with diminished efficiency. He still complains of pain but his emotional reaction to it is reduced. His wife expressed forcibly the view that such destruction of a personality was quite unjustified but his son thought that though a high price had been paid, his suffering was definitely less.

I consider this a poor result; certainly the distress which totally disabled him has been relieved and we know of no other way in which it could have been; that does not make standard leucotomy any more than a thoroughly unsatisfactory way of dealing with intractable pain which is not due to incurable malignant disease.

The result of the second operation was good in 3 cases:

A 42 year old woman, stable, energetic and somewhat obsessional, whose hypertension, abnormal EEG, dilated ventricular system and psychological test results all suggested an organic basis for her severe involutional hypochondriasis, was only moderately helped by an open rostral leucotomy (often an inadequate operation) and later made almost symptom free by standard leucotomy, with comparatively little damage to her previously well integrated personality.

The diagnosis was uncertain in the case of a serious, hard working bank clerk of 30, who had been regarded as a simple schizophrenic; from childhood he had repeated chest and ear, nose and throat infections. For years life seemed boring and without interest and recurrent depression and headaches put him off work for months at a time from 21. At 29 he was in hospital, listless, complaining of constant headache, lack of concentration and embarrassment at what others might think of him. He became depersonalized after 3 E.C.T.; insulin made him feel worse. Rostral leucotomy made no apparent difference. Eight months later bilateral standard leucotomy lifted his anergic depression and in the 8 months since he has had no headaches. Though irritable and inclined to row with his father, with whom he has never been on good terms, the personality changes are not as marked as in many who have had 2 leucotomies. He takes an intelligent interest in world affairs and has read the first 4 volumes of Churchill's *War Memoirs* since standard leucotomy. The hurdle of returning to work has not (8 months later) been surmounted and his slick, unselfcritical and inaccurate responses to sensorial tests suggest that he is unlikely to be able to work at his previous standard. There is nothing now to suggest schizophrenia.

The other good result is more important:

A 42 year old housewife, a sociable person of extraverted personality, gave up her work as a milliner at 21 to care for her elderly parents. At 29, 3 months after they died, soon after each other, she married a cousin and was never really well from that time; fear of collapsing and of being alone prevented her going out and a thyroidectomy for supposed thyrotoxicosis only made her worse. Prolonged psychotherapy and physical treatments were unavailing. Behind a kindly front she was seething with indignation against her sister, whose illegitimate child she brought up, and with reactive disgust at herself. Rostral leucotomy relieved her tension but her behaviour was unchanged, though she was more irritable. Ten months later standard leucotomy made her bland and dull and it was not long before she was able to travel by 'bus for the first time in 14 years. At follow up nearly 2 years later she had grown plump and was giggly and rather fatuous, voicing her thoughts without concern for their effect on others. Her housework fully occupies all her days; she can no longer read since she cannot understand what she reads. She could not take 7 serially from 100 and her responses to questions about the meaning of proverbs were entirely concrete. She sometimes misused nouns (e.g. calling a grate a "drain"). Patient and husband call this result "a complete success", and he rather likes the severe frontal lobe deficit syndrome.

In another social setting personality deficits as marked as in this case might well have proved disastrous and comparable deficits in a woman of 29 have ruined a marriage.

She is a nice person and quite unable to understand why her husband finds her dull, but, as he says, "she never starts a sentence with 'I think' " and has the objective mentality referred to by Golla (1946). She is so much dominated by the immediate present that she never enquires about her father, to whom she was devoted and who lives at a distance, and can often be heard singing about her work within a few minutes of being desperately distressed by her husband's impatience and lack of affection for her; "she is not the woman I married", he said; I have not heard such a comment made by any relative of a patient who had uncomplicated rostral leucotomy.

A woman of 33 has been relieved of most of her tense preoccupation with death, and is even able to work at a job which requires speed in handling figures; it is fortunate that her husband is sufficiently robust to tolerate the emotionally flat, inefficient and inert person she has become for there is now no possibility of her being a companion to him.

Both of these cases rate as fair results; two other cases also rate fair, mainly because personality deficits spoil what would otherwise be good results.

A 65 year old man, in his second depressive breakdown, was ultimately relieved of illness, but has a lack of restraint which permitted him to expose himself to his young grand-daughter, and considerable intellectual impairment.

In the case of a 49 year old man whose depression apparently fluctuated with the Addisonian anaemia from which he suffered two leucotomies were done before his anaemia had been adequately treated and his recovery may be due to sufficient liver treatment rather than to operation. He has a marked personality change of characteristic type; formerly a scientific assistant in a laboratory he is now employed as a dish-washer in a canteen.

Two other comparatively young women have been virtually destroyed by the standard operation; both are now epileptic and likely to remain permanently in a mental hospital. It is possible that the functional effects of the lesion are, as a result of some such process as Hebb (1949) envisages, much more extensive than the probable anatomical extent of the lesion would suggest; certainly there was nothing unusual in the post-operative course of either to suggest that the anatomical extent of the incision was anything but the standard cut intended. One case is given as an example:

A married woman of 36, brought up in poverty and seriously handicapped by recurrent chest illnesses following pneumonia at 5, was timid and frightened of others. She tried to do domestic and factory work but had often to give up because of her physical health, and, against advice, had 2 children. For 9 years she had worried excessively, was too fearful to travel on buses, or even, sometimes, to leave her home, and her husband had to be released from the army to look after her. She carried on with increasing difficulty, tense, nagging and with occasional outbursts of temper. She was better in hospital but after open rostral leucotomy was little different. Nearly 2 years later standard leucotomy was done and for 10 days she was inert and doubly incontinent. At a rehabilitation centre she was symptom-free but when she went home she did no housework, often did not get up till midday and dressed no more than once a week. Slovenly and dirty in her personal habits, rudely outspoken and explosively irritable, she lived entirely in the present and totally lacked initiative. If told to do something she did it but nothing more. She was aware of her incapacitating inertia but insisted that her inability to do things was not just laziness. She described her psychic experience in metaphorical terms "I'm tied up in a room and I can't get out; it is dark . . . my mind is quite blank. I feel like I had a room full of furniture and it has been emptied and I feel it still has furniture in it . . . my mind is in there and I can't get it out . . . I can't make my mind work"; but when asked about the "dark room" she treated it concretely and said "it can't be a cellar, we haven't got a cellar; I can't find the door . . . we have no dark rooms in the house". She took no pleasure in anything. Ultimately it became necessary for her to remain in a mental hospital where the ordered life and constant encouragement to do things hides the gross disorganization of her personality. A single fit occurred 7 months after rostral leucotomy and she has had about 6 fits since the standard operation. She and her relatives all regret the operation.

The results in 22 cases show that though standard leucotomy may relieve symptoms where rostral leucotomy does not (and the relief even in these cases is rarely complete) the personality deficits may be appalling, at any rate in younger and vulnerable personalities. They suggest that if rostral leucotomy fails in cases which appeared to be suitable the answer is unlikely to be found in standard leucotomy. The capacity of this operation to do harm is such that the indications for it must be definite; it is too dangerous a procedure to employ merely because we cannot think of anything else to do.

Unilateral standard leucotomy might seem to be a suitable second operation if a rostral cut fails. With only 3 cases in this series, 1 of whom was better partly as a result of improvement in social conditions, there is too little evidence on which to base an opinion.

It may sometimes be that rostral leucotomy is inadequate because the incision is less than intended on one or both sides; if on both sides then a unilateral standard operation may well prove inadequate too, and if on one side only there is an even chance of making the cut on the side where there is already sufficient damage. So, on the whole, I do not regard unilateral standard leucotomy as a good second operation.

It is more likely that the answer, if surgical at all, will be found in an operation directed elsewhere, perhaps at the thalamus.

These strictures on standard leucotomy should not be extended unduly. There is less evidence of serious personality damage in those cases in which the operation is most often done, the chronic schizophrenics; it is, however, necessary to ask seriously whether failure of rostral leucotomy in patients with well preserved personalities, particularly if they are "inadequate", is because the case has been wrongly regarded as suitable for treatment by surgery or because ancillary psychotherapy or social case work has been neglected, rather than because the surgery was not sufficiently extensive. Though McKissock (1951) is undoubtedly right when he says that blind rostral leucotomy can always be followed by a more extensive section later the evidence presented here suggests that it is but rarely that it should be so followed, at least by a standard cut. The higher incidence of epilepsy after second operations (Freeman, 1953a) should also lead to additional caution in recommending them.

Freeman (1953b) has almost abandoned standard leucotomy in favour of transorbital, and Greenblatt *et al.* (1953) find a "bimedial" operation gives better results in chronic schizophrenics than the "bilateral" (standard) operation.

Sargant (1953) has long maintained that the more worried you are about doing a leucotomy because the personality remains good, the better will be the result. Ström-Olsen and Tow (1949) state that the more the patient is endowed in the first place with "spiritual quality", or for that matter with any higher qualities, the worse is the relative outcome in the end for that particular patient. These two views are reconcilable: it is standard leucotomy, on which Ström-Olsen and Tow reported, which can be so destructive of "spiritual quality". Limited operations, with which Sargant has had greater experience, and as experience with rostral leucotomy confirms (Pippard, 1955) are rarely destructive in this way, and it is the better personalities who derive most help from the reduction in tension they give.

Summary

The results of second leucotomies are described in 27 cases. Whilst a more extensive prefrontal cut than rostral leucotomy may relieve symptoms the personality deficits will inevitably be larger; they may be comparatively unimportant after standard leucotomy in

schizophrenics, but in inadequate, vulnerable psychoneurotics are usually serious. Of 19 cases who had bilateral standard leucotomy as a second operation, only 3 are considered good results, and one of these only because her husband likes her with marked frontal lobe deficits. Failure of rostral leucotomy in a psychoneurotic patient should lead to doubt whether surgery is the proper treatment for that case, rather than to more extensive leucotomy. Standard leucotomy in the plane of the coronal suture is too destructive an operation for such cases.

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THE FOLLOW-UP OF A CHILD GUIDANCE CLINIC POPULATION

By

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I—Introduction

We all know cases who have got better and we like to think that we played a part in causing their improvement. To prove this is, however, a very different matter. We have all read the follow-up studies based on a carefully selected group of cases where the authors report on those whom they could trace—but what of the untraced? At times, an overall survey of one's case material may reveal facts unnoticed in the preoccupation with the day to day clinical work.

In an attempt to look at their work in a more impersonal fashion the Staff of the Bristol Child Guidance Clinic decided to take all those cases who first attended in 1946 and see what had happened to them by 1951. For purposes of comparison each case was assessed on a five-point scale for the complex variable Adjustment-Maladjustment, these terms being used to cover an individual's reaction to his environment and to himself, no matter whether the reactions were shown in the social, intellectual, emotional or physical field.

In order to make the assessment as objective as possible, the following precautions were taken:

(i) The field workers and judges were not members of the clinic staff.

(ii) The data referred to well-defined aspects of behaviour, e.g. how many friends, rather than sociability.

(iii) The facts, though gathered in slightly different ways, were of the same type and presented to the judges in the same way, thus eliminating variation due as much to the difference in methods of presentation as to changes in the individual.

(iv) Whenever possible the results were expressed in numerical form so that statistical methods could be applied and the reliability and validity of the assessment estimated.

II—Method

A record form (App. I) was devised. The items were selected on the basis that they were important in the child's adjustment, were capable of objective assessment and had, for the most part, been recorded in the original clinic histories.

As we wished eventually to use the method (devised by C.J.B.) for comparing referred and non-referred cases, the complete group of 340 cases referred for the first time in 1946, the first post-war year, was chosen for the sample. Eight of these cases were found to have married and were excluded from the assessment procedure as the interview method was inappropriate.

Tracing

As a first approach a letter was sent to the last known address of the parents. A card with only an identifying number and a stamped addressed envelope were enclosed. The card asked if the child was fit and well, how he or she got on at school or work and how he or she got on with the family. The present address was also asked for. This card was not meant to provide follow-up material but solely to trace change of address.

Two fourth-year university students in psychology filled up a record form for every case using the 1946 diagnostic interviews as their only source of data. They visited all addresses in Bristol obtained through the reply cards and if the card had not been returned, the last known address. Enquiries were also made at the house on either side. If the neighbours knew the present address and it was in Bristol this new address was also visited. They filled up an identical record form based on an interview, if possible, with the mother, as she had usually been the informant in 1946. They did not consult the original record before visiting.

When children were resident in institutions a questionnaire was sent to a responsible person there and the interview form completed from it. At the same time parents living outside Bristol were sent a card asking whether they would consent to complete a questionnaire. If they agreed a questionnaire was sent and, when returned, an interview form was completed from it. If the parents refused or did not return the questionnaire no further action was taken at this stage.

By the end of August, 1951, after two months interviewing, 202 cases had been traced. These constitute the Main Sample (MS). It was felt, however, that the problem of cases difficult to trace needed further study and accordingly in 1952 a woman sociology graduate carried out further tracing of two sub-samples of the 138 originally not traced. Sample A was a random sub-sample of 35 cases. Sample B consisted of 28 cases who had Bristol addresses but who had not been visited earlier either owing to the isolation of their addresses or because they had had to be traced through several addresses and were located too late for inclusion in the MS. Sample A, being random, included certain cases found in Sample B.

When the interviewers had completed their work there were two forms for each child, identifiable by code number but otherwise indistinguishable though, in certain cases, age or details of work might have indicated that it could be only a follow-up record.

Judging

A University lecturer in Psychology, a Medical Officer at a Mental Hospital, a Headmaster of a Special School, a Psychiatric Social Worker and a Youth Employment Officer were then invited to act as judges. Each judge was provided with a set of instructions and then given a copy of each record that had been obtained. The records were arranged in the same random order for each judge. Thirty identical pairs of records were included so that reliability could be measured. Each judge, working separately, rated every record on a five-point scale. Neither the purpose nor the design of the study was known to the judges.

Treatment of Results

When the five sets of records were returned there were ten ratings for each child, five for 1946, five for 1951. As the mean scatter of the individual judges'

ratings corresponded closely the five ratings for each individual were added together, giving pooled ratings for 1946 and 1951 with a possible range from 5–25. The difference between these two pooled ratings gave a Pooled Improvement Rating for each child, with a possible range from +20 to −20.

III—Results—Method

Qualitative

The interviewers found the majority of informants very co-operative, and in only two cases was information refused. There was no objective check on the reliability of the informants but they appeared to be as reliable as in ordinary clinic work.

The possibility that the greater knowledge about younger children still at home might influence the assessment was considered. This was checked upon statistically and we consider that it is unlikely that the ratings were biassed by this factor.

The record form was found simple to use and adequate for a pilot survey. For further work, the form would be modified in the following ways:

(i) Enlarge the list of symptoms and, where possible, rate separately for extent and frequency, e.g. stammers in all, most, specific situations: stammers over most, few words.

(ii) Include information on known physical disabilities.

(iii) Extend the "Home" section, if possible, with more factual categories.

Quantitative; Reliability and Validity

(i) Reliability of interviewers:

Statistical checks of their work were possible and revealed no significant differences.

(ii) Reliability of judges:

To check the reliability of the individual judges, about 30 record sheets, which were duplicates of cases already included except for minor changes in I.Q. and age, were mixed with the MS records. In fact the judges did not recognize these "duplicates".

The reliability of the judges as measured by the correlation of their ratings on these pairs was:

Judge	A.	r = ·934**	n = 31
	B.	r = ·927**	n = 26
	C.	r = ·846**	n = 35
	D.	r = ·520**	n = 35
	E.	r = ·800**	n = 31

If the ratings on these duplicate records are pooled the reliability for the judges' pooled ratings becomes—r = ·941** n = 24.§

This result confirms the desirability of employing more than one judge. The reliability is raised above that of the most reliable single judge.

(iii) Reliability of judges after lapse of time:

When the A and B samples were judged a year after the MS, duplicates of records previously judged (25 for 1946 and 10 for 1951) were introduced to measure the consistency of the judges after a period of time.

§ The varying numbers here are due to the fact that some duplicates were mislaid.

** Indicates significant at p = ·01 level.

* Indicates significant at p = ·05 level.

The reliability of the individual judges after a lapse of a year was:

Judge A. r=·770** n=35
B. r=·724** n=35
C. r=·866** n=35
D. r=·601** n=35
E. r=·520** n=35

If the ratings on these duplicate records are pooled the reliability for the judges' pooled ratings after a lapse of a year becomes r=·886** n=35. On their second rating of the records the judges rated slightly but not significantly higher. This applies to both 1946 and 1951 records.

It may be concluded that in spite of variability between and within the judges' ratings the reliability of the method of assessment, both immediately and after a lapse of a year, was high and quite comparable with reliability in other methods of case study.

(iv) Agreement between judges:

In both the MS and the A and B samples the distributions of the individual judges' ratings were more or less the same. Mean and standard deviations were computed for each judge and were found not to differ significantly between the judges.

As this was so the average inter-correlation between all the judges could be calculated. (Kelly. Guilford. Psychometric Methods, p. 370.)

In the MS these average inter-correlations were:

$\bar{r}$ pq=·745** for the 1946 records. 202 records. 5 judges.
$\bar{r}$ pq=·685** for the 1951 records. 202 records. 5 judges.

In the A+B samples combined, which were assessed a year later, the average inter-correlations are:

$\bar{r}$ pq=·453** for the 1946 records. 141 records. 5 judges.
$\bar{r}$ pq=·661** for the 1952 records. 61 records. 5 judges.

(v) Disagreement between judges:

There were occasional differences of 1 or 2 points, differences of 3 or 4 were exceptional. Disagreements of this type are part of the rating procedure and are a reflection of the contribution of each judges' training and outlook to the final assessment.

More questionable, however, are differences of direction. When, for instance, a small Pooled Improvement Rating is due to some judges rating the individual improved and some rating him deteriorated. Forty-five such cases were found in the Whole Sample of 243 cases including all those cases where one judge or more had disagreed in direction with one or more of the others, whether or not some judges had rated no change, the latter being taken to be disagreement in degree. These 45 "direction disagreement" cases were found not to have influenced findings in the Whole Sample.

(vi) Validation of 1946 Pooled Ratings:

An attempt was made to check the validity of the method by comparison with an external criterion. Judge A. was familiar with the layout of clinic case papers and rated 30 cases randomly selected, using the records of the same diagnostic interviews as had been used earlier by the interviewers. The correlation between his ratings and the pooled rating of the judges was

r=·640** n=30. The correlation between this same judge's rating from case papers and from record forms was r=·815** n=28. Since this judge's reliability on the MS was very high it can be concluded that so far as validation against case papers is concerned the method is adequate.

(vii) Validation of the 1951 Pooled Ratings:

Thirty-five cases were selected randomly from the MS and 23 of these children were interviewed by one of us (R.F.B.) the majority at the clinic, the parents not being seen. Some interviews took place nearly a year after the follow-up interview.

The results were much less satisfactory in this check, the correlation being r=(·090) NS n=23 which is not significant.

Two cases were of special interest. In one the boy had appeared in the Juvenile Court in the interval between the follow-up assessment and the psychiatric interview and this probably accounted for the psychiatrist's rating of 2 versus the judge's agreed rating of 5. In the second case a boy (aged 17·3 years I.Q. 129) was rated low by the judges (1·6) and high (5) by the psychiatrist. Investigations revealed that the record sheet showed a number of aggressive pastimes and recent psychosomatic symptoms. The symptoms were not disclosed by the boy to the psychiatrist who considered that as the aggressive tendencies appeared to be successfully sublimated (collecting antique weapons and fencing club) he could not be considered maladjusted, though liable to react excessively to any unusual stress. Apart from the difference in information available the judges and the psychiatrist differed as to the degree to which prognosis was to be considered.

However, if these two cases, where special circumstance intervened, are omitted the correlation becomes r=·623** n=21.

These two discrepant cases together with the time-lag between interviews and the small number of cases interviewed by the psychiatrist, indicate that validity in this study cannot be taken as proven. In any further study we should use more than one psychiatric rating as an external criterion, both child and parent would be interviewed and validation would be carried out immediately.

The extreme difficulty of validation in this field may be illustrated by the fact that using similar rating scales, and rating new cases presented at our weekly case conferences, agreement between 6 members of the clinic staff, two psychiatrists, two psychologists and two psychiatric social workers, varied from r=·844** n=24 to r=·534** n=24.

IV—The "Not Traced"

(a) *Main Sample and Population*

The Main Sample consisted of 202 cases. Could one assume that the remaining 40 per cent. resembled those traced? The MS was compared with those who at that time were not traced, referred to hereafter as the Not Yet Traced (NYT).

The MS was representative of the year's cases as regards age and intelligence. As might be expected the mean age of those NYT was higher than of those in the MS. This difference was significant.

Mean age on referral. MS = 9·6 n=202
Mean age on referral. NYT=10·6 n=138
t=2·331* Df=338

The NYT differed in referral source, significantly more coming from "Other Agencies". Substantially more treatment cases were found in the MS. More surprising was the finding that fewer females and more males appeared in the MS than was to be expected by chance.

(b) *Random Sample of the Not Yet Traced (Sample A)*

This sub-sample was a random one of 35 cases drawn from the 138 cases remaining after the first sampling.

After some difficulty we were able to trace and interview 24 cases from this sub-sample (17 per cent. of the NYT). These 24 proved to be characteristic of the 35 cases originally taken, at least so far as age, sex, intelligence, referral source and disposal were concerned. In fact, all 35 cases were traced but not all could be interviewed and assessed. Of the 11 thus traced but not assessed; 1 had been killed in Korea, 1 was married and 2 had emigrated to Australia. The parents refused to give information in 2 further cases and 2 cases were in a Borstal institution and could not be interviewed. In the remaining 3 cases we had information indicating that they were doing well but the evidence was insufficient for a record form to be adequately completed.

The 24 cases in Sample A thus obtained were not significantly different from the NYT in age, intelligence, sex, referral source or disposal.

The sample had, however, a significantly lower 1946 Pooled Rating than the MS:

MS Mean 1946 PR=15·401
Sample A, Obtained Mean 1946 PR=13·542
t=2·877** Df=241

The difference between means of Pooled Improvement Rating, was not significant.

MS Mean PIR=4·084
Sample A, Obtained Mean PIR=4·542
t=(·522) NS Df=241

It can be stated that Sample A did not differ significantly from the NYT and in improvement was not significantly different from the MS.

The fact that Sample A as obtained has a significantly lower 1946 Pooled Rating is of interest and suggests that the NYT cases might have been more maladjusted on referral.

(c) *Second Sample of Those Traced in Bristol (Sample B)*

This sub-sample consisted of cases who had been traced provisionally to Bristol addresses, but who for various reasons had not been included in the MS. Of 28 such cases 24 were assessed. Four cases could not be traced by the MS criterion of tracing.

Sample B thus obtained was compared with the NYT and was not significantly different as regards intelligence, sex, referral source or disposal.

It was found however to be significantly younger. This result is to be expected in view of the fact that these cases would have been able to have been included in the MS had time allowed, and thus show the same tendency as the MS in this respect. In fact, the mean age of Sample B as obtained is not significantly different from that of the MS. As with Sample A the mean 1946 Pooled Rating is significantly lower than that of the MS and the mean Pooled Improvement Rating not significantly different.

(*d*) *The Finally Not Traced*

The Whole Sample consisted of 243 cases, the sum of the MS and Samples A and B. The remainder are the Not Traced (NT).

Unfortunately it cannot be said, even of this study, that those individuals

in the NT were solely those who were most difficult to trace, for other factors such as marriage, lack of co-operation, difficulty of making contact, all entered in.

The length of time available for locating cases will always be a factor in determining the group of "untraced cases". We were surprisingly fortunate in being able to locate all the cases in what had been drawn as a random sample of the NYT but, even there, two cases who had emigrated could not be assessed, for the sample had to be judged before arrangements could be made to have questionnaires completed in Australia.

The following findings regarding the NT may be of use in other surveys:

(*i*) They tend to be older. WS Mean age on referral = 9·6. NT Mean age on referral = 11·2. $t = 3 \cdot 269^{**}$ Df = 338.

(*ii*) There are few treatment cases, this being probably due to the fact that the time lapse between the follow-up and the last date the child was seen was under 3 years.

(*iii*) Intelligence level is not associated with presence in the NT.

(*iv*) The proportion of juvenile court cases was higher in the NT though not significantly so.

(*v*) Other Agency referrals are significantly more frequent in the NT: School Medical referrals in the WS.

(*vi*) The NT contains a significantly greater proportion of girls. It has not been possible to determine whether this sex difference is entirely due to local conditions or may have a more general application.

V—Results—Follow-up

The pooled ratings show an improvement in the cases on follow-up in 1951 within the MS.

Pooled Ratings for 1946 records n = 15·401 SD = 3·59 n = 202
Pooled Ratings for 1951 records n = 19·485 SD = 4·83 n = 202
Correlation between the Pooled Ratings in 1946–1951 $r = +\cdot 184^{**}$

The difference between the means 4·084, is significant at $p = \cdot 01$. This improvement does not tell us anything about the work of the clinic unless we have a control group with which to compare results.

Before turning to the breakdown of the follow-up results we would remind readers that we were working with histories taken five years previously. Some of the characteristics we would like to have studied, for instance the effect of the stability of the mother, had been inadequately recorded in 1946. We could not assume that the absence of an entry necessarily meant that the entry would have been "normal". Further, no attempt was made to check the mother's original statements, e.g. that she had, in fact, had a prolonged labour. Despite these limitations a wide range of characteristics were known sufficiently accurately to make useful comparisons possible.

The method of dealing with "not known" categories should be explained. A table was constructed splitting the sample into variable A/Not A and into variable B Known/Not Known. If there was no significant association between variable A and B Known/Not Known the "not known" were discarded. If there was a significant association the "not known" were added into the cells such that the difference between the cells was reduced to a minimum.

Besides source of referral, sex, age, and intelligence (App. II), we had adequate information on abnormal or difficult birth, feeding difficulties, toilet training, early separation from mother, position in family (App. II) (recorded as only, eldest, mid-sibling or youngest), family situation (adopted, fostered, institutional, step-parent, and parent deceased).

Reasons for referral were classified according to List C of The National Association for Mental Health Inter-Clinic Child Guidance Committee (App. III).

Disposal categories were taken from the Clinic "status at closure", i.e. Treatment Improved, Treatment "in statu quo". Supervision Improved, Supervision I.S.Q. and Consultation Only. Treatments closed through lack of co-operation were few in number and are mostly included in the second category, unless it was clear that treatment had achieved some positive result.

In this paper the results of only the more important comparisons will be referred to, in particular those which are considered to be applicable to the work of other clinics.

Differences Associated with Sex

In our sample the usual preponderance of males occurred—163 boys to 80 girls.

No significant associations were found between sex and 1946 Pooled Ratings, Pooled Improvement Ratings, intelligence, early difficulties of development, position in family or source of referral.

The girls in the sample were significantly older than the boys ($p < \cdot 05$). There was also a significant association between girls and abnormal family situations, i.e. adopted, foster, institutional, step-parent or parent deceased and this was true even after the Juvenile Court referrals had been removed. This association in part is due to the significantly high proportion of girls with deceased fathers: there were only 3 cases in all with deceased mothers.

	Male	Female	Total	
Deceased Father	7	9	16	Whole Sample excluding
Family Situation "Normal"	107	44	151	Outside Bristol and Juvenile Court referrals
	114	53	167	$\chi^2 = 4 \cdot 908^*$ Df=1

There was no significant deviation from chance occurrence when sex was compared with the reasons for referral. Eight boys were referred for truancy, 6 boys for masturbation, but no girl was referred for either of these symptoms. These figures are too small to apply statistical tests.

One quite unexpected finding was that sex is associated with disposal; this is dealt with later.

Differences Associated with Age

The older children tended to have lower 1946 Pooled Ratings and tended to improve more than the younger children. This is in conflict with the generally accepted idea that treatment or advice is more effective with younger children. In the Whole Sample, less Juvenile Court cases, the following correlations were found:

1946 Pooled Rating and Age	$r = -\cdot 216^{**}$	n=210
Pooled Improvement Rating and Age	$r = +\cdot 226^{**}$	n=210

Differences Associated with Intelligence

There was no significant correlation between intelligence and either 1946 Pooled Rating or Pooled Improvement Rating in the Whole Sample. In the Treatment Group there were the same findings, a result which does not support the practice of treating only those children with higher I.Q.s.

Differences Associated with Early Difficulties of Development

Early difficulties of development were classified under four headings:

(1) Difficult Birth—41 cases.

(Instrumental 16; Breech or Face Presentation 5; Six or more weeks premature 7; Others, e.g. jaundice, long labour 13.)

(2) Difficult Feeding—53 cases. (Food fads after the age of three are not included.)

(Sudden loss of milk 14; Bottle fed and unsatisfied over long period 16; Refusal of breast or bottle 9; Weaning difficulties 7; Others, e.g. slowness, tantrums before age 2, 5.)

(3) Difficult Toilet Training—51 cases.

(Tantrums—difficulty over "potting" 13; Very slow in training 10; Never fully established 28, of which 17 were referred for enuresis.)

(4) Early Separation—54 cases. Early separation was split into separation occurring under 2 years and separation between 2–6 years old. In fact there was no significant difference between these two groups as regards 1946 Pooled Rating and Pooled Improvement Rating so that they have been added to make an Early Separation (under 6) group. Under age 2 all separations from natural mother included, between 2 and 6 all separations from mother for more than one month, less if there was confirmatory evidence of trauma.

(Hospitalization 23; Evacuation, Adoption, Fostering 13; Illness, death or desertion of mother 9; Other 9.)

It is a rather striking finding of our survey that the scaled assessments of general adjustment, made without any theoretical preconceptions of the importance of these factors, should yet show significant differences when the sample is split according to these four headings.

Early Separation is significantly associated with abnormal family situations so we shall deal first with Difficult Birth, Difficult Feeding and Difficult Toilet Training groups only, which are not complicated by this factor to a significant extent. Comparing the three groups: (*i*) the "All Normal", where each of these factors was known to be normal, (*ii*) "Not Known", where these factors were possibly normal but for whom definite evidence of normality was lacking for one or more factors but none was definitely abnormal, (*iii*) "Difficult" where there was definite evidence of difficulty in one or more factors:

(i)	All Normal	Mean 1946 PR=15·000	Mean PIR=5·162	n= 68
(ii)	Not Known	Mean 1946 PR=14·514	Mean PIR=4·814	n=105
(iii)	Difficult	Mean 1946 PR=15·571	Mean PIR=2·886	n= 70

Analysis of variance shows the differences in 1946 Pooled Rating to be not significant, and the differences in Pooled Improvement Rating to be highly significant ($p<\cdot01$).

Difficult Feeding and Difficult Toilet Training together affect the individual to a far greater extent than either one by itself.

(*a*)	Normal Feeding and Normal Toilet Training	Mean PIR= 5·123	n=81
(*b*)	Difficult Feeding and Normal Toilet Training	Mean PIR= 4·358	n=26
(*c*)	Normal Feeding and Difficult Toilet Training	Mean PIR= 3·00	n=27
(*d*)	Difficult Feeding and Difficult Toilet Training	Mean PIR=−·800	n=15

Groups *a* and *b* are significantly different from group *d* at the ·01 level: group *c* from group *d* at the ·05 level and group *a* from group *c* at the ·05 level. The differences between group *a* and group *b* and between group *b* and group *c* are not significant.

The four factors will now be considered separately.

Comparing Difficult Births with the remainder there is no significant difference in 1946 Pooled Rating but there is a significant difference in Pooled Improvement Rating.

Difficult Birth	Mean PIR=2·561	n= 41
Normal plus Not Known Birth	Mean PIR=4·386	n=202
t=2·247*	Df=241	

The same findings occur with Difficult Feeding; the difference in 1946 Pooled Rating is not significant, the difference in Pooled Improvement Rating is significant.

Difficult Feeding	Mean PIR=2·471	n= 51
Normal plus Not Known Feeding	Mean PIR=4·386	n=192

t=2·395* Df=241

If the Difficult Toilet Training group is analysed by itself the 1946 Pooled Ratings were significantly higher and there was a significantly lower Pooled Improvement Rating. If, however, those cases referred for excretory disorders are removed, also eleven cases of enuresis not referred for this symptom, then the same effect of Difficult Toilet Training appears as in the group for Difficult Birth and for Difficult Feeding.

Difficult Toilet Training (less those referred as Enuretics and those not referred for this symptom)	Mean PIR=—·895	n= 19
Normal Toilet Training plus Not Known Toilet Training (less those referred as Enuretics and those Enuretics not referred for this symptom)	Mean PIR=4·839	n=176

t=3·990** Df=191

It was found that there was a tendency for Difficult Birth to predispose the child towards the adverse effects of Difficult Feeding, Difficult Toilet Training and Early Separation though not at a statistically significant level.

In our sample, first, i.e. oldest and only children, occurred significantly more often in the Difficult Birth, Feeding and Toilet Training group, a finding that confirms the common, but seldom substantiated, view that first children have more to contend with than subsequent siblings.

First Children and Early Difficulties

	Normal	Difficult	Total	
Older and Only Children	29	62	91	
Youngest and Mid-siblings	39	41	80	χ^2=5·065* Df=1 (Not known omitted)
	68	103	171	

We conclude therefore that Difficulties in birth, feeding and toilet training do not produce more severe maladjustment but improvement is less, or at least slower. Also first children will tend to show less, or slower, improvement.

The Early Separation group shows a significantly lower 1946 Pooled Rating than the remainder of the sample, but the Pooled Improvement Ratings are not significantly different. However, this finding is considerably influenced by the cases adopted, fostered and institutionalized in all of which there was early separation.

When such cases, where early separation is in fact a part of a family break-up, are excluded there are no significant differences between the Separated, Separation Not Known, and Not Separated groups. The tendency of the means is the same as for the other early difficulty groups. We are not able to show, therefore, in our sample, that early separation alone and not accompanied by family break-up, has a definite effect on later maladjustment.

Early Separation appeared to be significantly associated with those referred as "unmanageable". However, this was in fact due to the relatively large

number of adopted, foster, step or institution children in this category, nearly all of whom had experienced early separation.

We did not find early separation to be associated with any other characteristic studied. In particular there was no higher proportion of early separated among the Juvenile Court referrals as compared with all other referrals.

Differences Associated with Position in Family

When position in family was analysed it was found that oldest and only children tended ($p < \cdot 10$) to be more frequently referred on account of fears than youngest or mid-siblings. They were less frequently referred for stealing ($p < \cdot 10$). Only children were less likely to be referred on account of excretory disorders ($p < \cdot 10$). Oldest, youngest and mid-siblings did not differ with regard to 1946 Pooled Ratings but oldest tended ($p < \cdot 10$) to show less improvement than youngest or mid-siblings.

Differences Associated with Disposal

In the sample of 243 cases there were 166 consultation cases. Sixty-five children were taken on with their parents for treatment (eclectic psychotherapy, at least once per week) and 12 cases were supervised (parent and usually child being seen at 4–6 weeks intervals). As the supervision group is so small comparisons have only been made between the Treatment and the Not Treatment groups where there was no significant difference as regards 1946 Pooled Ratings and Pooled Improvement Ratings although the Treatment group tended to show slightly more improvement.

Treatment	Mean 1946 PR=15·015 n= 65	Mean PIR=4·631
Not Treatment	Mean 1946 PR=15·140 n=178	Mean PIR=3·876
t=(·250) NS Df=241	t=(1·084) NS Df=241	

At first sight this might suggest that treatment had achieved little. However, it should be pointed out that treatment cases were easier to locate as they had often been in touch with the clinic within the last three years: in fact, 91 per cent. of treatment cases were included in the sample. If it had been possible to compare all treatment cases with all non-treated the tendency to greater improvement in the treated cases might have been more marked and in fact significant. Further, cases are selected for treatment precisely for the reason that without treatment they are considered to be unlikely to improve.

With the Treatment group there was no significant difference between Short, Medium and Long Term Treatment cases.§ Nor was there a significant difference in 1946 Pooled Rating or Pooled Improvement Rating between cases closed Treatment Improved (47) and Treatment ISQ (18).

There was, however, one quite unexpected finding within the Treatment group namely that the sexes were dealt with differently. This question of sex differentiation came up in other ways even with regard to the returning of the preliminary tracing cards when parents of boys returned the card more often than parents of girls.

Population (less Outside Bristol cases)

	Male	Female	Total	
Card returned by Parent	103	41	144	
Card not returned	94	73	167	$\chi^2=7\cdot735^{**}$ Df=1
Total	197	114	311	
Card returned by G.P.O.	16	13	29	

§ Short=under ten sessions. Medium=ten to fifteen sessions. Long=over sixteen sessions.

The girls in the Treatment Group showed a significantly higher 1946 Pooled Rating than the boys but no significant difference as regards Pooled Improvement Rating:

Boys	Mean 1946 PR=14·481 n=52	Mean PIR=3·923
Girls	Mean 1946 PR=17·154 n=13	Mean PIR=4·808
	t=2·948** Df=63	t=(·634) NS Df=63

Further while the ratio of boys to girls referred was 2 : 1 the ratio treated was 4 : 1. This difference, significant in the whole sample, remains so when Outside Bristol cases, a biassed group both with regard to sex and treatment, are removed.

Whole Sample (less Outside Bristol cases)

	Treated	Not Treated	Total	
Boys	50	103	153	
Girls	13	59	72	$\chi^2=5·194^*$ $p<·02$ Df=1
	63	162	225	

When this group was broken up into the three main divisions for referral symptoms, namely, Nervous Disorders, Habit Disorders and Physical Symptoms, and Behaviour Disorders, it was found that the association of differential treatment was only significant for the second group; Habit Disorders and Physical Symptoms.

Habit Disorders and Physical Symptoms Referral Group

	Treatment	No Treatment	Total	
Boys	21	25	46	
Girls	3	20	23	χ^2 7·187** Df=1
	24	45	69	

We have, so far, been unable to find a satisfactory explanation of why it is harder for girls with such symptoms to obtain treatment The fact that we might avoid treating adolescent girls or girls from broken homes has been gone into and the association between treatment and sex is still significant ($p<·05$) for children from normal homes and for children aged 7–12 on referral. The tendency remains, though at a lower level ($p<·10$) even when the cases are split according to the psychiatrist making the diagnosis, one of whom at the time was male, the other female.

This particular finding may be of only local importance but as the sexes do not appear in equal proportions in the Child Guidance population throughout the country it may be of interest elsewhere.

Differences Associated with Bristol Child Guidance Clinic Administration

A survey of this type also throws light on local arrangements and we analysed our results in terms of referral source, time awaiting consultation, time between consultation and treatment and re-referral. It allowed us to see whether the full range of problems was being referred from each source or whether there was a high degree of, possibly unconscious, pre-selection. These findings being largely the result of such local factors as public relation-

ships of the Clinic, professional interests of the Staff, etc., are not being given in this paper.

VI. Summary

1. A relatively simple interview record and rating method was designed to be used in a five-year follow-up of Child Guidance cases.

2. The method was found to be satisfactory in operation and as reliable as most personality assessments. Certain modifications would be introduced if the method were to be used in a more extended survey.

3. The results of studying not traced cases emphasizes that in any enquiry of this kind the not traced should be as intensively studied as the traced, for in our sample some of the differences between these groups were significant.

4. The sample improved between 1946 and 1951.

5. Early Difficulties in Birth, Feeding and Toilet Training do not affect maladjustment on referral but make for slower, or less, improvement and this holds when these factors are considered separately. Difficult Birth tends to predispose the child towards the adverse effects of Difficult Feeding, Toilet Training and Early Separation. Difficult Feeding and Difficult Toilet Training occurring together affect the individual to a far greater extent than either occurring by itself.

6. A number of sex differences were found in our sample. Girls were older on referral than boys. Girls taken on for treatment tended to be less maladjusted than boys. Proportionately fewer girls were treated, a difference due partly to a tendency not to treat girls with habit disorders and other physical symptoms. The reasons for referral did not differ proportionately between the sexes.

7. Only children and oldest siblings are found more frequently in the Difficult Birth, Difficult Feeding and Difficult Toilet Training Group than other children, not, however, to a significant extent when these factors are considered separately. Oldest siblings show a tendency to less or slower improvement than other siblings.

8. The results give no clear evidence of the effect of treatment but suggest that had it been possible to trace the whole population there might have been evidence for treatment leading to more or quicker improvement.

9. This survey fulfilled its limited purpose of studying our clinic population five years after its referral. The reasons for the overall improvement were not the subject of this survey and would require the comparison of a clinic population with an equivalent unreferred population. In our opinion, an objective and reasonably economical study can be made of the results of Child Guidance practice and methods of this kind could be applied to normal or selected control groups.

Acknowledgments

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APPENDIX I

Record Form

Bristol Child Guidance Clinic — Confidential

No. Age Sex I.Q. Informant

Symptoms

Type:

Wetting	Spitefulness	Deceit	Suicide—threat attempt
Soiling	Nailbiting	Timidity	Stealing
Masturbation	Tics	Tempers	Truancy
Stammering	Nightmares	Withdrawal	*Other offences*
Destructiveness	Insomnia	Daydreaming	

Treatment:

Hosp. Mental Hosp. G.P. C.G.C. S.M.O. *Other*

Length of Treatment Days Wks. Mnths. Yrs.

School

Type (R)	Secondary Modern or Primary	Technical	Grammar	Approved	Special ESN/D/B/OA	*Other*
Likes	Very much	Quite	Indif.	Dislikes	Hates	

Appendix I—*continued*

STAYS AWAY	Alm. never	Seldom	Now and then	Quite often	Great deal	
TROUBLE	Alm. never	Seldom	Now and then	Quite often	Great deal	
REPORT	Works well	Average	Badly			
SCHOOL FRIENDS	Many	Few	1–2	None		
COMPLAINTS	Lazy	No concentration	Always fooling	Doesn't mix	Passive	*Other*

WORK

CURRENT JOB			CURRENT UNEM.	PERIOD UNEM.		*Reason*	
PREV. UNEM.		*No.*	*Length*	*Reason*			
NAT. SERVICE	Current	Past	None	*Reason*	Army	RAF	Navy
PROSPECTS	Definite	Some idea	No idea	EARNINGS			
PREV. JOBS			REASONS FOR LEAVING				
No.							
SATISFACTION	Likes very much		Quite	Indif.	Dislikes	Hates	
STAYS AWAY	Almost never		Seldom	Now and then	Quite often	Great deal	

HOME

AT HOME	AWAY	*Reason*	CONTACTS HOME	Frequently	Infrequently	Never
PREVIOUS ABSENCES		*No.*	*Length*	*Reason*		
HELPS AT HOME	Frequently	Infrequently	Never			
RELATION WITH PARENTS (F. & M.)	Very good	Good	Fair	Poor	Bad	
RELATION WITH SIBLINGS	Very good	Good	Fair	Poor	Bad	
RELATION WITH INDIVIDUAL SIBLINGS	Very much	Quite	Indifferent	Dislikes	Hates	
FAMILY OUTINGS	Great deal	Quite often	Now and then	Seldom	Almost never	
CONTACT OUTSIDE FAMILIES	Great deal	Quite often	Now and then	Seldom	Almost never	

LEISURE

NUMBER EVENINGS OUT	CINEMA VISITS	Never	Less than 1 p.w.	1 p.w.	2 p.w.	3 or 3+
ACTIVITIES	Home	Out	*Specific activities*	(2 p.w.)		

SOCIAL

FRIENDS (B & G)	Many	Few	1–2	None	ADULT FRIENDS	
AGES OF FRIENDS	Much older	Older	Same age	Younger	Much younger	
CHANGES OF FRIENDS (B & G)	Never	Occasionally	Often	GANG MEMBER	Leads	Mucks in	Follows
FRIENDS TO HOME	Yes	No	ATT. TO VISITORS	Sociable	Indifferent	Unsociable

PERSONAL

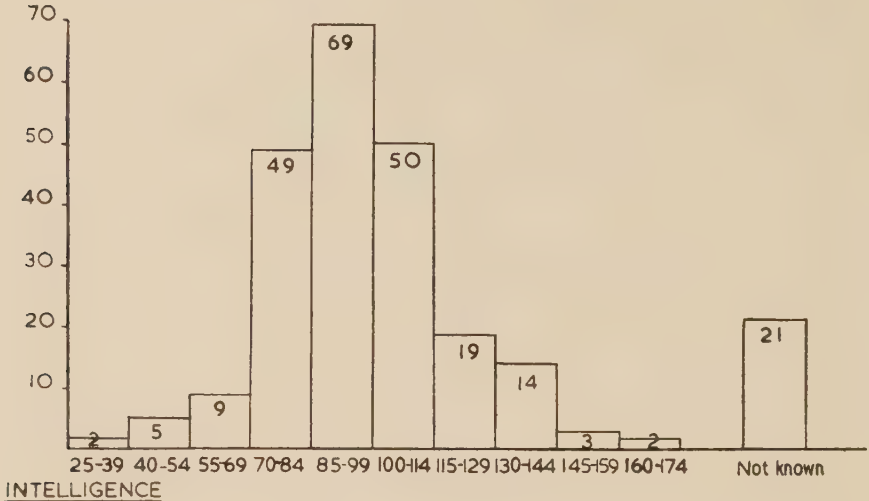
Single	Engaged	Steady B G friend		Broken Engagement	*Other*
PSYCHOSOMATIC (rate)	Headache	Migraine		Fatigue Digestive	*Other*
	Asthma	Hayfever		Rheumatism Epilepsy	
ACCIDENTS	*No.*	*When*	*Type*		
ILLNESSES	*No.*	*When*	*Type*		
WORRIES	*Health*		*Others*		

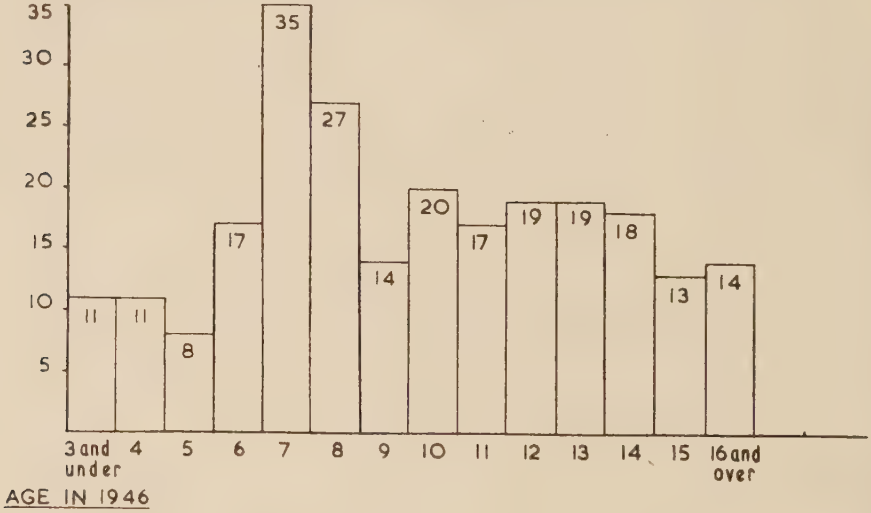
CLUBS

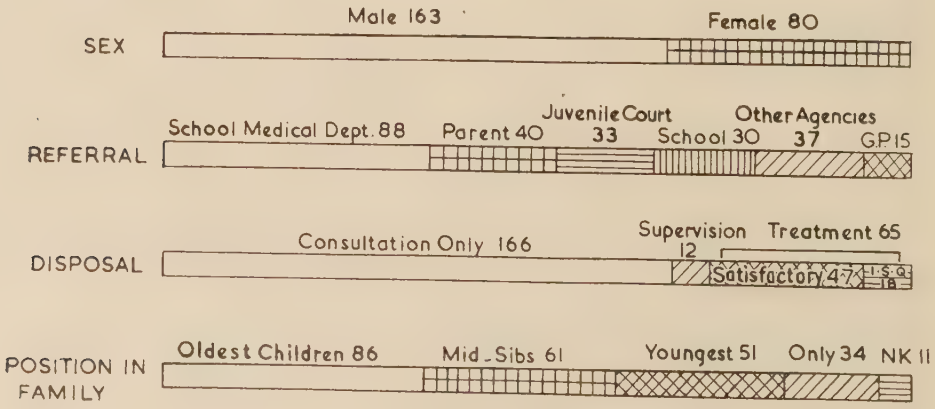
No.	*Type*	*Frequency*	Leader	Mucks in	Follows

APPENDIX II

Distributions in the Whole Sample, 1946







APPENDIX III

Reason for referral:

The Classification used is according to the list issued by the Inter-Clinic Child Guidance Conference before the war; only the major reason given at the time of referral was listed:

I. Nervous Disorders:		*including:*	*Boys*	*Girls*	*Total*
1. Fears	—	anxiety, phobias, timidity, over-sensitivity	13	8	21
2. Seclusiveness	—	unsociability, solitariness ..	2	0	2
3. Depression	—	brooding, melancholy periods ..	2	1	3
4. Excitability	—	over-activity	1	0	1
5. Apathy	—	lethargy, unresponsiveness, no interests	1	2	3
					30

II. Habit Disorders and Physical Symptoms:		*including:*	*Boys*	*Girls*	*Total*
1. Speech disorders	—	stammering, speech defects, hysterical aphonia, inability to speak	6	2	8
2. Sleep disorders	—	night-terrors, sleep-walking, insomnia, talking in sleep ..	5	2	7
3. Movement disorders	—	twitching, tics, habit-spasms, head-banging, thumb-sucking, nail-biting	6	2	8
4. Feeding disorders	—	refusal of food, food-fads, nervous vomiting, putting things in mouth	1	1	2
5. Excretory disorders	—	constipation, enuresis, faecal incontinence, refusal to use lavatory	26	13	39
6. Nervous pains and Paralyses	—	hysterical paralyses, nervous dyspepsia, pains in limbs, headache, functional deafness	0	3	3
7. Fits	—	epilepsy, hysterical fits, periods of unconsciousness, loss of memory	2	0	2
					69

III. Behaviour Disorders:		*including:*	*Boys*	*Girls*	*Total*
1. Unmanageable	—	disobedience, beyond control, persistent negativism, defiance, refusal to work or go to school	19	11	30
2. Temper	—	tantrums, anger, screaming fits ..	7	2	9
3. Aggressiveness	—	bullying, destructiveness, spitefulness, cruelty	5	1	6
4. Jealous behaviour	—		1	0	1
5. Demanding attention	—		3	2	5
6. Stealing	—	begging	20	11	31
7. Lying and romancing	—		2	0	2
8. Truancy, attention	—	wandering, staying out late ..	8	0	8
9. Sex difficulty attention	—	masturbation, sex play, homosexuality	6	0	6
10. Adolescent sex	—		1	1	2
					100

IV. Educational and Vocational Difficulties:		*including:*	*Boys*	*Girls*	*Total*
1. Backwardness attention	—	mental retardation, school failure	12	6	18
2. Inability to concentrate	—	day-dreaming, inattention ..	1	2	3
3. Special disabilities	—	high-frequency deafness, word-blindness, handedness ..	1	0	1
4. Miscellaneous	—		12	10	22
					44

THE DETECTION OF PSYCHOLOGICAL VULNERABILITY IN STUDENTS

By

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PARNELL (1951) reported that 76 men undergraduates at Oxford had lost a full term's residence on account of psychological ill health in the period of three years from 1 January, 1947 to 31 December, 1949. Psychological ill health had caused 52·5 per cent. of all prolonged absence through illness, a fact which emphasized the need for more detailed study of the causes and possibility of prevention of psychological disturbance. As an indication of minimal current prevalence of such disturbance, it may be reported that 59 Oxford students in need of psychiatric help were referred by their general practitioners to the Warneford and Park Hospitals in twelve months from 1 April, 1953 to 31 March, 1954: these figures take no account of the numbers treated elsewhere; but the evidence as a whole shows that, as found in 1951, mental upset is still the most important cause of ill health in Oxford students.

Information derived from a comparison of somatotype, electroencephalographic, psychological and psychiatric findings upon patients and healthy controls is summarized in this paper. It shows that, despite a probable bias in the controls, significant differences can be detected between the two samples. Some of these differences were sufficiently marked to form the basis for a simple heuristic method of detecting vulnerability.

THE SAMPLES

Both patient and control series consisted of 100 Oxford students speaking English as their first language and between the ages of 18 and 28 when first seen. Both series were similarly examined by somatotype, electroencephalograph and a battery of four psychological tests of which two only are relevant to the present paper. Both series, moreover, were interviewed psychiatrically; the patients frequently and extensively; the controls on one occasion only for 50–80 minutes. As the patient series contained four Americans, only the first four American controls volunteering were included.

The 100 patients were referred consecutively by general practitioners to the

Warneford Hospital for Mental Disorders, the Park Hospital for Functional Nervous Disorders or the Park Hospital Out-patient Department, and were either under treatment at the outset of the investigation in April, 1951, or were referred between then and April, 1954. Six were replaced by the next six attenders: one because of complicating head injuries; the other five failing for clinical reasons to complete sufficient tests.

The 100 voluntary controls, all freshmen of 1953–54, came from three colleges. The proportion of the annual entry of each college volunteering was respectively 64 per cent., 30 per cent. and 29 per cent., making an overall proportion volunteering of 42·3 per cent. Of the 123 students who volunteered, the first 100 of appropriate age and with English as their native language, were chosen as the control group.

The fact that more than 40 per cent. of the total entry volunteered, implies that the majority of the controls were healthy young men, though the possibility of bias on grounds such as public-spiritedness or interest in psychology cannot be excluded.

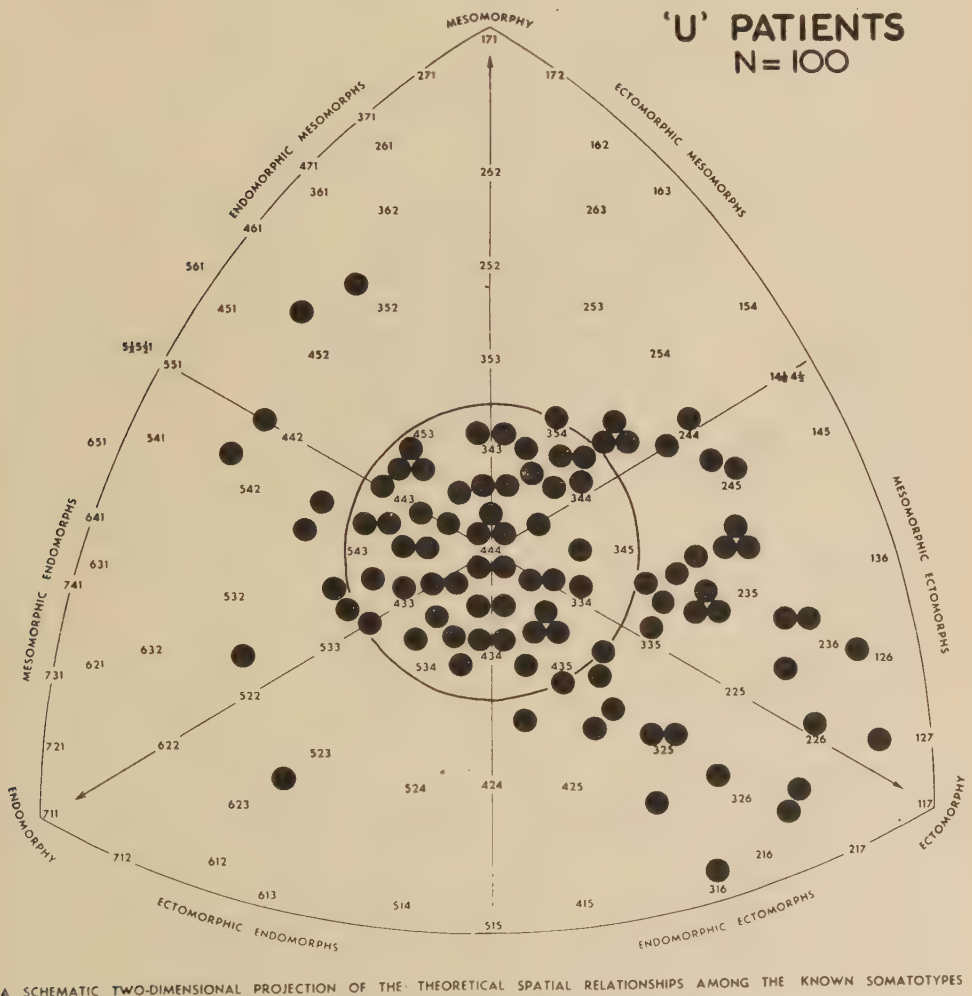

FIG. 1.—Somatotype distribution of 100 consecutive undergraduate patients referred by their general practitioner for psychiatric treatment.

Somatotype Bias Amongst the Volunteers

Somatotype evidence will now be presented from a comparison of both patients and controls with 405 students derived from a pilot health service from 1947–50 and similarly typed to show that a bias among the controls did exist towards physiques similar to those of patients.

Method

Sheldon's photoscopic method of somatotyping was compared with results reached independently by means of physical anthropometry before the final

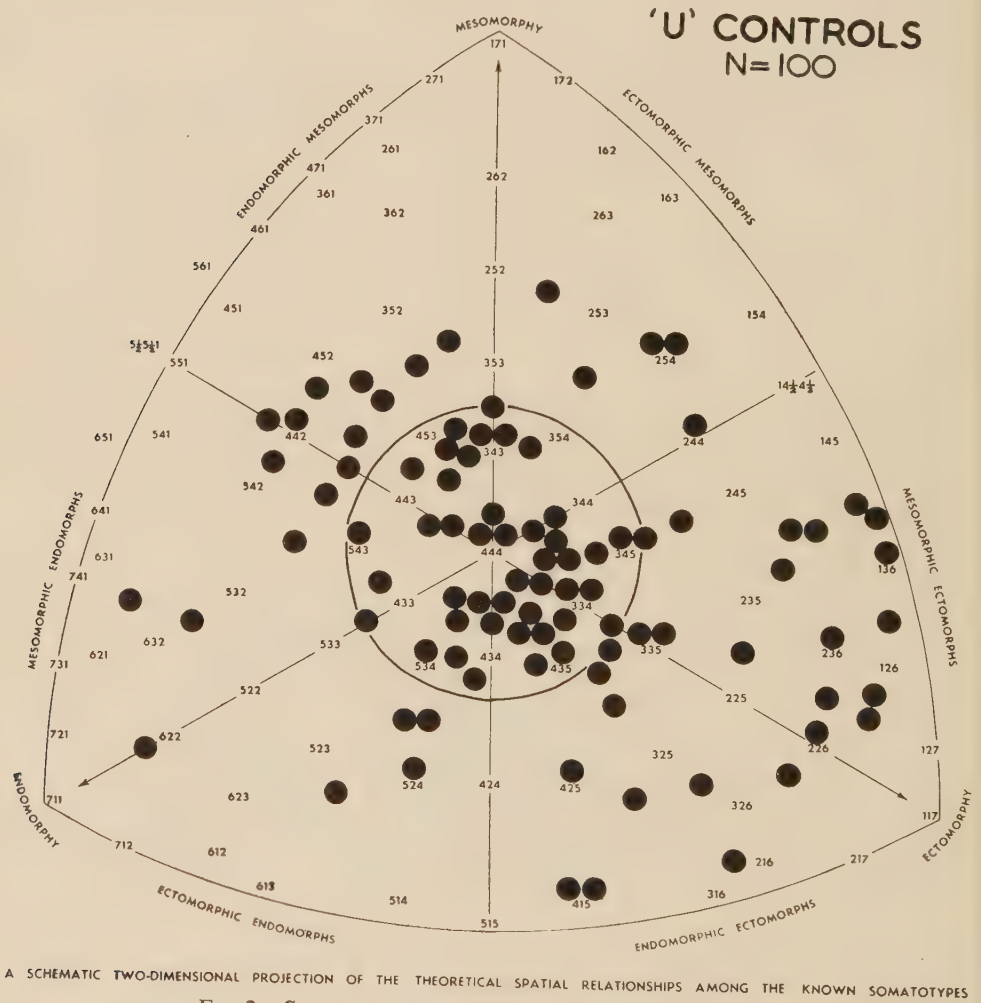

Fig. 2.—Somatotype distribution of 100 volunteer controls.

3-figure index of physiques was decided upon. The objective figure derived from physical anthropometry ensured the procedure greater internal consistency (Parnell, 1954).

The orthodox 3-dimensional somatotype chart devised by Sheldon is divided into six main sectors of dominance which, together with the central 444's, gives 13 main somatotype groups (see Fig. 1). Concise notation is used

to describe the regions, e.g. 453, 343, for central endomorphic mesomorphs, and mesomorphs with shared secondary dominance. Peripheral types of similar dominance are noted as P453, 343, the prefix "P" preventing confusion with central types. The notation for other sectors of dominance follows suit.

Samples

Figures 1 and 2 depict the somatotype distribution of patients and controls. The application of these comparative distributions to the delineation of the vulnerability scale will be described later.

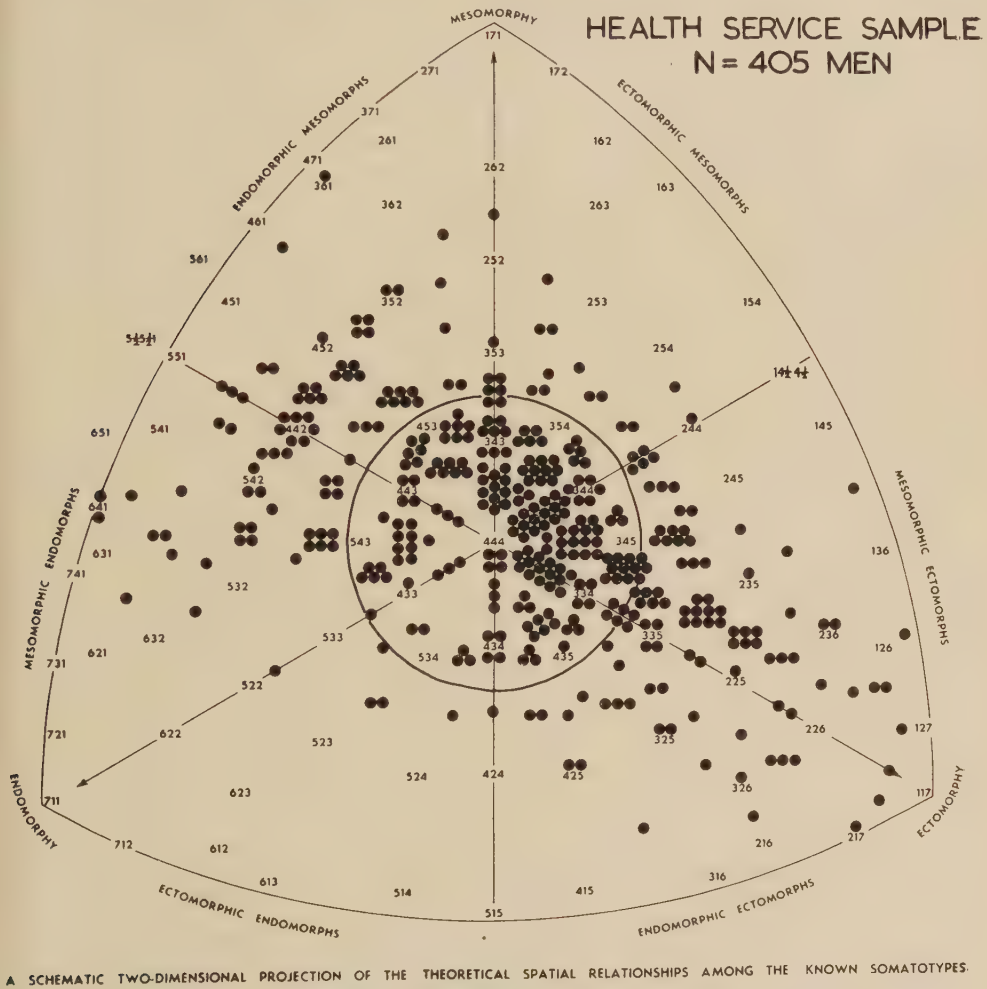

FIG. 3.—Somatotype distribution of 405 men attending a pilot health service 1947–1950.

The bias in body build of the controls can be measured against the distribution of the 405 pilot health service students (see Fig. 3). This health service sample is considered a more satisfactory standard of the normal distribution of physiques of Oxford students for three reasons; first, it was larger, secondly the volunteer rate (70 per cent.) was higher, and thirdly, a check carried out by

Tanner (1952) on a large part of the sample, revealed that athletic physiques were fairly represented.

The comparative frequency of the volunteers and patients compared in the somatotype groups with the health service sample is shown in Table I.

TABLE I

Comparative Prevalence Ratios of Undergraduate Psychiatric Patients, Psychological Volunteer Testees and Health Service Attenders by Somatotype Groups

Central		Nos. and Percentages				Prevalence Ratio			Significant at 5 per cent. level*		
		1 S.H.S.		2 Vol.	3 Pts.	1 S.H.S.	2 Vol.	3 Pts.	D1–2	D1–3	D2–3
		n	%	n=%	n=%						
534	433	10	2·5	6	8	100	243	324		*	
543	443	22	5·4	4	10	100	74	184			
453	343	49	12·1	8	9	100	66	74			
354	344	45	11·1	3	8	100	27	72	*		
345	334	56	13·8	12	4	100	87	29		*	*
435	434	23	5·7	9	9	100	158	158			
444		4	1·0	3	5	100	300	501			
Central Subtotal		209	51·6	45	53	100	87	103			
Peripheral											
534	433	5	1·2	6	1	100	483	84			
543	443	45	11·1	8	7	100	72	63			
453	343	38	9·4	6	2	100	64	21		*	
354	344	18	4·4	6	5	100	135	113			
345	334	63	15·6	19	20	100	122	129			
435	434	27	6·7	10	12	100	150	180			
Peripheral Subtotal		196	48·4	55	47	100	113	97			
Central and Peripheral											
534	433	15	3·7	12	9	100	324	243	*		
543	443	67	16·6	12	17	100	72	103			
453	343	87	21·5	14	11	100	65	51	*	*	
354	344	63	15·6	9	13	100	58	84	*		
345	334	119	29·4	31	24	100	105	82			
435	434	50	12·4	19	21	100	154	170		*	
444		4	1·0	3	5	100	300	501			
Total		405	100·2	100	100						

The actual frequency is divided by the expected frequency based on the health service sample and the quotient multiplied by 100 to give a comparative ratio. A ratio of 100 is therefore recorded where the frequency of a given group of somatotypes is identical with that in the health service sample; ratios above or below will be found where the prevalence in the patients or controls series is higher or lower respectively (see Figs. 4 and 5).

Findings

These findings demonstrate not only which physical types mainly avoided and which succumbed to psychological breakdown, but also which type of student was especially interested in taking part in the experiment.

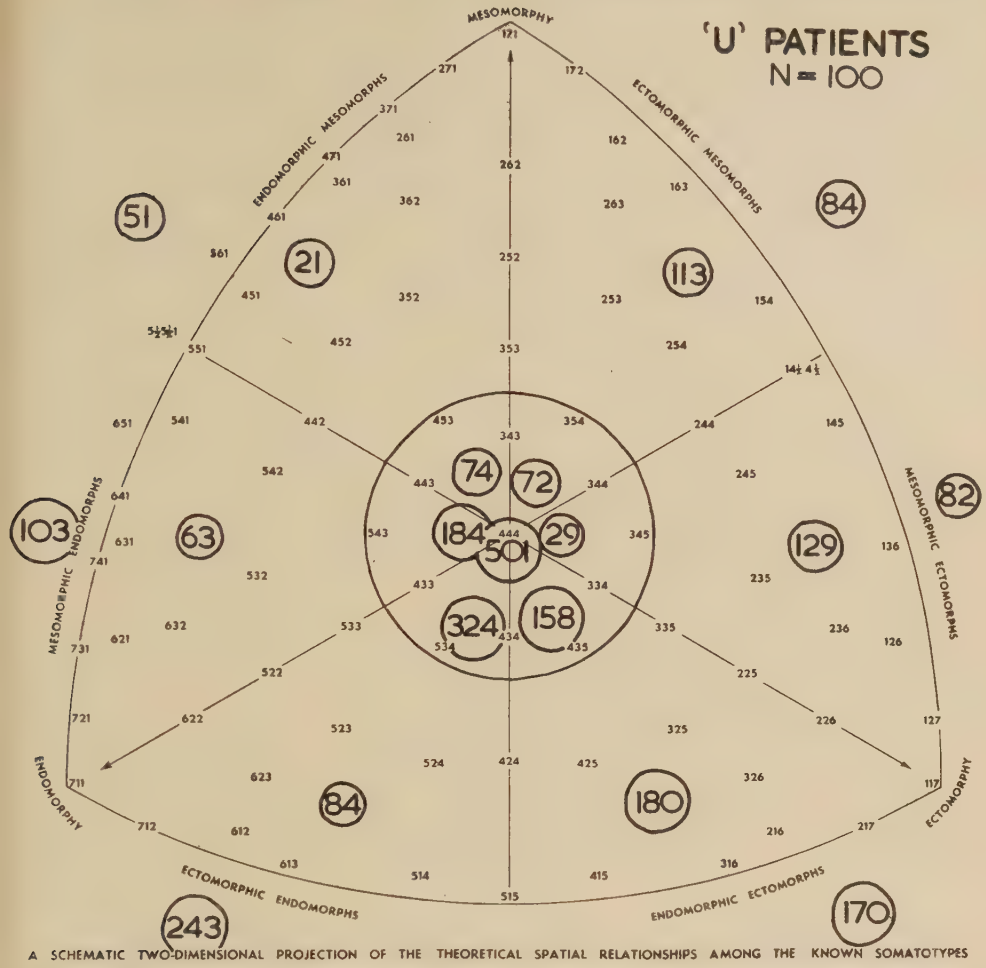

FIG. 4.—Comparative ratios of somatotype prevalence among the patients. The expected ratio would be 100 in the health service sample.

Mesopenes of all types (C.P. 435, 434, 534, 433) were found significantly more often among the patients

$$\left(\frac{\text{Diff. in proportion}}{\text{S.E. Diff.}} = 2{\cdot}8\right)$$

than among the health service sample; they also volunteered significantly more often for control testing

$$\left(\frac{\text{Diff. in proportion}}{\text{S.E. Diff.}} = 3{\cdot}1\right).$$

Mesomorphs on the other hand (C.P. 453, 343, 354 and 344), if central and peripheral ones are taken together, not only appeared significantly less often as patients

$$\left(\frac{\text{Diff. in proportion}}{\text{S.E. Diff.}} = 2{\cdot}7\right),$$

but they also volunteered significantly less often as controls

$$\left(\frac{\text{Diff. in proportion}}{\text{S.E. Diff.}} = 2{\cdot}9\right).$$

In contradistinction, however, endomorphic mesomorphs (a region, incidentally, where medical students congregate (Parnell, 1953)), had less than average interest in the experiment and only a small casualty rate, while central ectomorphic mesomorphs, who co-operated least well in the experiment, nevertheless showed relatively greater liability to breakdown.

Table I also reveals the need to distinguish between central and peripheral types of the same dominance. Taking ectomorphic endomorphs (534m 433)

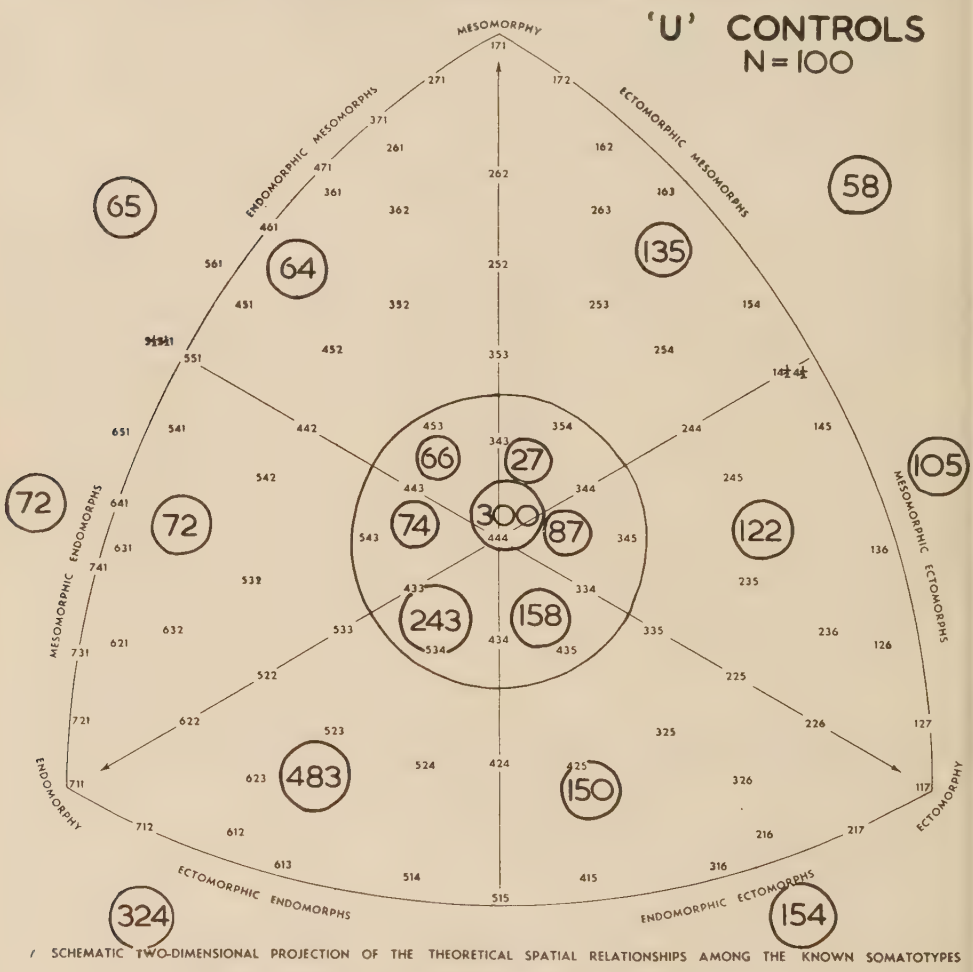

FIG. 5.—Comparative somatotype prevalence among the volunteer controls.

as an example, it may be seen that they volunteered more frequently than all other groups, the peripheral ones if anything more often than the central ones; but it was the central ones who most frequently became patients. If as a further example mesomorphic ectomorphs are considered, they showed near average disposition to volunteer, but while the comparative ratio for patients at the periphery is rather above expectation, that for central types (C 345, 334) is very low. This highly stable "eastern-central" area on the somatotype map is one of the most densely populated regions in the university sample (Parnell, 1953) though, incidentally, it is one with comparatively poor academic record (Parnell, 1954b).

In general summary it may be said that the volunteer controls appeared to be closer in physique to the patients than to the health service sample. The assumption is therefore permissible that the differences found below between the patients and controls would tend to be enhanced among the more divergent physiques of the University at large.

Factors Differentiating Patients and Controls

Medical and personal histories, recorded at psychiatric interview, will next be examined to discover factors differentiating patients from controls. Electroencephalographic and psychological test results will be studied subsequently and the best differentiating information gathered together to develop scales of vulnerability.

Medical and Personal History

(*a*) Insignificant Factors

As already mentioned the age range was the same for patients and controls and one may add that the age distribution was also similar.

Table II lists the percentage prevalence of factors which failed to show significant difference between 100 student patients and 100 controls.

Table II

The Percentage Frequency of Factors Failing to Differentiate Between 100 Student Patients and 100 Controls

	Patients (Per cent.)	Controls (Per cent.)
Father's Occupation:		
Professional	18	26
Scholastic	10	10
Business Director	29	21
Managerial, foreman, etc.	27	32
Traders, miners, labourers, etc.	16	11
Schools Attended:		
State-aided day only	49	51
Private day	10	9
Boarding	41	40
University Status:		
Scholar	29	21
Exhibitioner	5	8
Commoner with F.E.T.S., State, County or other Grant	38	43
Commoner without State Grant	11	9
Post-graduate or graduate elsewhere	17	19
Financial Security of Subject:		
Number who worried about money, were in debt, or admitted difficulty in making ends meet	4	4
National Service and War Service:		
Completed	56	49
Deferred	28	36
Unfit	13	10
Others not liable	3	5

From Table II it may further be seen that no significant difference was encountered in social class judged from the father's occupation, type of school attended, university status, financial aid, financial security or national service.

Social inferiority, therefore, financial stress, the unsettling effect of national service, or, alternatively, the immaturity of those who have not yet done it, create no significant danger of psychological breakdown. This is not to say that none of these factors ever contribute to distress: it means merely that by themselves they cannot be considered important causes of breakdown.

Religious Interests

A waning interest in religion has been cited as a cause of breakdown. The actual proportion of patients now agnostic, undecided or otherwise deviated in religious affiliation from that of their upbringing, was just significantly greater than the proportion of controls (see Table III). But because the controls were seen only shortly after arrival at university the difference could be explained by longer opportunity for change in Oxford's iconoclastic atmosphere, an hypothesis confirmed in Table IV by the figures of change in religious interest according to the year of residence.

TABLE III

Religious Interests

Interest	Patients	Controls
Agnostic now	25	14
Undecided now	7	10
Others who changed from religion of upbringing	17	10
Total changing	49	34

TABLE IV

Changes in Religious Interest According to Year of Residence

	Patients			Controls		
	Number	No. Having Changed	Per cent.	Number	No. Having Changed	Per cent.
1st year	19	6	32	100	34	34
2nd year	26	11	42	—	—	—
3rd year or later years	47	24	51	—	—	—
Post-graduate	8	8	100	—	—	—

(*b*) SIGNIFICANT FACTORS IN THE HISTORY

Faculties

The percentage distribution of students according to faculty is given in Table V, to which the distribution has been added for the whole University, taken from the 1953 Calendar. There is a suggestion that men reading "Literae Humaniores" had a greater tendency to breakdown; the tendency is slight and the test of significance

$$\left(\frac{\text{Diff. in proportion}}{\text{S.E. Diff.}} = 1{\cdot}8\right)$$

reveals that it approaches, but does not reach the 5 per cent. level. Similar remarks apply to Geography. The least liability was found among student lawyers and linguists. Modern historians contributed a significantly small number of patients, but they contributed a similar small proportion to the control series too. The conclusion is reached that choice of faculty is not an important factor in breakdown.

TABLE V

Percentage Distribution of Students According to Faculty

Faculties	Patients n=100	Controls n=100	O.U. 1953 n=1603
Lit. Humaniores	15	7	9
Geography	6	3	3
Modern Languages	8	15	13
Jurisprudence	6	10	10
Theology	5	4	3
Medicine	5	8	4
Modern History	8	9	19

Faculties showing no difference of distribution have been omitted.

Previous Personal and Family History of Psychological Disturbance

Significantly more patients had suffered at an earlier period from psychological illness, but 80 per cent. had no previous experience of this kind (see Table VI). If a knowledge of previous upsets were to be obtained by Student Health Officers when a student starts his university course, this information could succeed in directing supervisory attention to only one fifth of those likely to need it. Likewise, evidence of mental disorder in the family history is significantly more common in the families of patients, but its comparatively infrequent

TABLE VI

	Patients (Per cent.)	Controls (Per cent.)
Previous Psychological Illness:		
None	80	98
Out-patients only	13	2
Mental hospital	7	0
Psychological Illness among Relatives:		
Nil known	61	81
Some relative afflicted	39	19
Direct	17	10
Collateral	15	7
Both direct and collateral	7	2
Parental Circumstances:		
Harmony now or when both parents were alive:		
Good harmony	52	71
Slight disharmony	19	12
Disharmony	20	9
Broken home:		
Separation by arrangement, legal separation or divorce	8	7
Mother died at birth of son	1	1
Relations of Subject with Family:		
Mildly disturbed:		
With father	26	9
With mother	30	4
With siblings	9	2
With family as whole	26	9
More severely disturbed:		
With father	16	2
With mother	11	3
With siblings	4	4
With family as whole	18	5
Total disturbed:		
With father	42	11
With mother	41	7
With siblings	13	6
With family as whole	44	14

occurrence renders it by itself almost useless for prediction. Moreover, bias may have been produced as a result of information supplied by parents of patients; for parents of controls were not interviewed.

Parental Circumstances

In assessing the significance of this factor, it must be understood that the information was derived from the subjects themselves; it is therefore possible that patients were more forthcoming than controls in admitting disharmony.

Although disharmony between the parents was admitted significantly more often among patients than among controls, over half the patients came from homes where no evidence of disharmony could be detected, and twenty-one controls had not broken down despite the presence of disharmony. "Broken homes" are sometimes thought to be equally damaging, but the incidence of homes broken by death, separation and divorce was not greater among patients than among controls, suggesting that continuing disharmony, or possibly the patient's idea that such disharmony exists, may matter more than an actual break.

Relations Between Subject and Family

Assessment of this was based on description of relationships afforded by patients and controls and, occasionally, in the case of patients, by their relatives. Greater knowledge of the patients, together with knowledge gained in some cases from analytical exploration of intimate personal affairs may therefore have biassed these figures. Moreover, the controls may have glossed over or repressed knowledge of disturbance.

The point of importance here, however, is that over 50 per cent. of the patients had reasonably serene relations with their parents and in less than 20 per cent. of the cases was there any severe disturbance. This factor has, therefore, only limited value in the assessment of vulnerability.

EEG Findings

Thirty-two per cent. of the 72 patients with EEG recordings gave "abnormal" records, i.e. they showed considerable theta activity at 4–7 c/s, delta waves at 1–3½ c/s, or an epileptic pattern of a well recognized form either at rest or on overbreathing. A small amount of bitemporal theta activity was accepted as within normal limits. By the same standards, 42 per cent. of controls were classed "abnormal". This difference is not significant statistically although it will no doubt be noted as departing in the "wrong" direction. Moreover, 12 per cent. of controls showed an epileptic pattern, none, however, giving a clinical history of epileptic attacks; and it is interesting here to record that in the student health service series of over 500 Oxford undergraduates only about half 1 per cent. suffered from clinically diagnosed grand mal or petit mal epilepsy. An additional finding of special interest was that as high a proportion as 19 per cent. of peripheral ectomorphs showed epileptic patterns in their EEG, whereas only 4·5 per cent. of endomorphs showed this characteristic.

It can be concluded that electroencephalography by itself is valueless in distinguishing students psychologically vulnerable from those who are not.

Tests of Intelligence and Honours Class Results

A.H.5 is a closed, time-limited test of high grade intelligence devised by Dr. Alice Heim (1947) of the M.R.C. Unit in Applied Psychology at Cambridge,

and divided into two parts, each occupying 20 minutes, Part I testing verbal and arithmetical reasoning, Part II with its visual bias, mainly non-verbal reasoning. The five grades A to E comprise descending levels of ability. The total score is obtained by direct addition of scores in each part.

TABLE VII

A.H.5 Test. Percentage Distribution of Test Grades Obtained by Patients and Controls

Grade	Patients (90)			Controls (100)		
	Part I	Part II	Total	Part I	Part II	Total
A	10	10	11	12	9	14
B	22	19	18	22	27	19
C	41	28	31	36	38	40
D	18	29	28	19	16	15
E	9	14	12	11	10	12

There is no significant difference in the three upper grades A–C; the difference between patients (40 per cent.) and controls (27 per cent.) placed in the lower two grades D–E on the total scores, although suggestive, is just below the 5 per cent. level of statistical significance. However, the difference in Part II at grades D–E between patients (43 per cent.) and controls (26 per cent.) appears significant. This is in line with the usual finding that a high proportion of patients with neurotic, psychotic and organic disorders show discrepancies between verbal and non-verbal ability.

The honours class results of these patients who have taken their final examinations are compared in Table VIII with figures for the University as a whole, taken from the University Calendar, 1953. No significant difference was found.

TABLE VIII

Honours Class Results

	Patients		O.U. 1953	
	No.	Per cent.	No.	Per cent.
1st Class Honours	7	12	121	9
2nd Class Honours	30	52	731	55
3rd Class Honours	18	31	411	31
4th Class Honours	3	5	70	5

The data from intelligence tests and examination class results appear to dispose, at least as far as Oxford is concerned, of two notions frequently advanced as common causes of breakdown. The first is that biological maladjustment is associated with extremely high or supernormal intelligence. The second is that failure in mental health arises from men with intelligence within the lower ranges encountered at the University being unable to survive the stress of academic demands and competition. Although some slight support might be claimed for this latter view from Part II of the intelligence test, it is not a significant factor in the test as a whole, there is a well accepted alternative explanation and, therefore, no reason to regard it as one of the commoner causes of breakdown.

The Establishment of a Vulnerability Scale

(*a*) The Minnesota Multiphasic Personality Inventory. Description and Methodology

According to Hathaway and McKinley (1943), authors of the M.M.P.I. Manual, this is a psychometric instrument designed to provide scores on the more important deviations of personality. The test material consists of 550 intimate personal statements, each printed on a separate card, which the subject is asked to sort into three categories indicating that he considers each statement either true or false about himself, or he cannot say.

From the sorting, nine characteristics of personality named after symptom complexes are objectively scored. Standard scores are used around a mean of 50 with one standard deviation equal to ten points, and a score of 70 (i.e. the mean+2 S.D.) is taken as a convenient criterion of abnormality. The nine characteristics have here been neglected: a score of 70 or more obtained on any one scale being employed to define abnormality.

Findings

Among 100 controls 33 per cent. were classified by this standard as abnormal. Among 93 patients 28 per cent. were classified as "normal". The total misclassification of 31 per cent. is higher than can usefully serve to discriminate the sick from the healthy.

(*b*) M.M.P.I. Combined with Somatotype

In an attempt to improve the discrimination, the scores were noted which distinguished best between patients and controls in separate areas of the somatotype chart. These areas are illustrated in Fig. 6: where for each zone the optimum score separating patients and controls has been entered. It would be unwise on the available data to attach too much importance to the precise levels and exact ranges of somatotype implied, but trends suggest for example that peripheral mesomorphic ectomorphs and mesomorphic endomorphs may score more than 70 and even as high as 80 without becoming patients, whereas among mesopenic ectomorphs scores as low as 65 are common among patients. As an indication of the improvement in discrimination between patients and controls brought about by using the relevant optimum M.M.P.I. score for each somatotype, only 19 per cent. of patients would be thought normal, only 18 per cent. of normals would be suspect patients. The total of 19 per cent. misclassified is significantly less than when the M.M.P.I. is used alone (31 per cent.).

Since a complete university intake of 700 students at Birmingham has been somatotyped in one week as part of the routine health assessment on entry, and since the M.M.P.I. may be taken as a written group examination occupying from 30 to 90 minutes and scored by clerks, there is no technical reason why these procedures should not be combined for screening new entrants. They cannot be claimed as highly efficient, but it should be remembered that among the patients considered, a certain proportion did not perform the M.M.P.I. until near full recovery; while among controls one or two seemed vulnerable and may have volunteered because they felt in need of help. Thus an upper limit with perhaps 10 per cent. misclassified might reasonably be expected on the present data.

(*c*) PSYCHIATRIC INTERVIEW

Object

To reduce misclassification further, ratings derived from a short psychiatric interview may be used. While it is impractical for all university entrants to be interviewed, it might be more feasible to interview those suspected vulnerable by the combination of M.M.P.I. and somatotype.

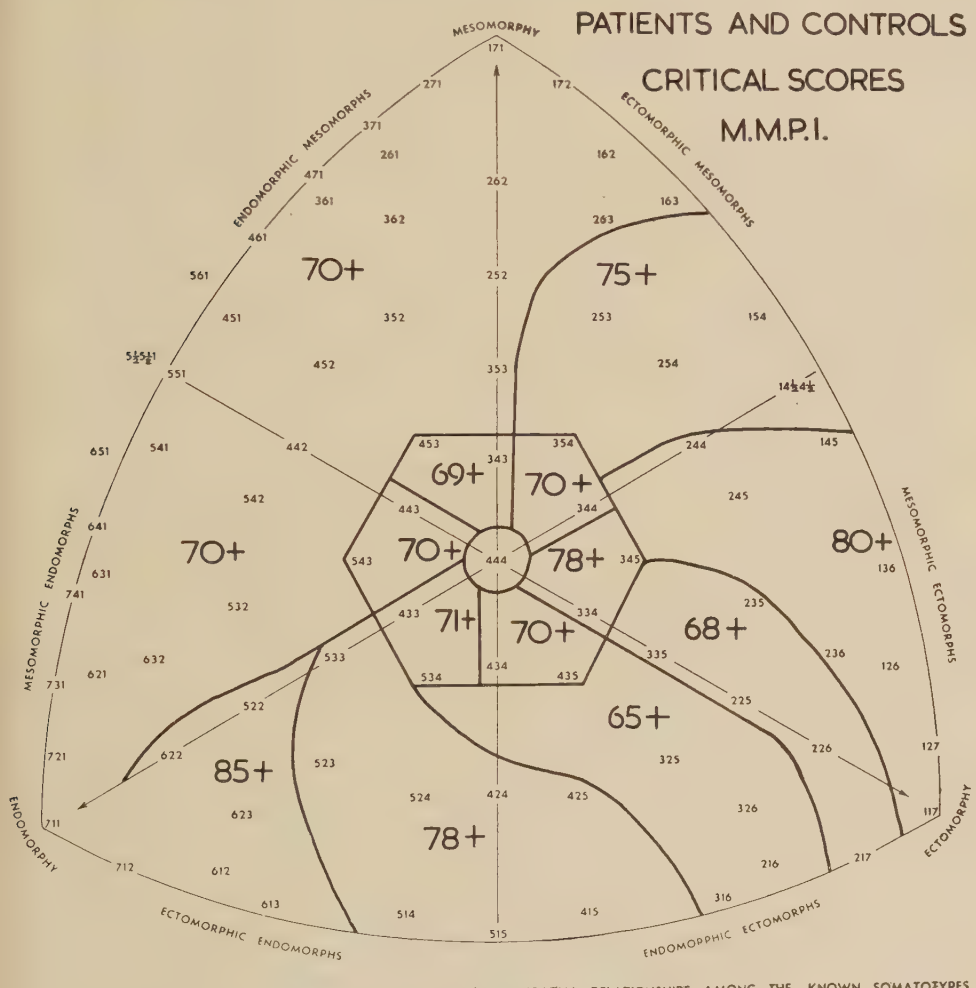

FIG. 6.—M.M.P.I. Best discriminating scores between patients and controls according to somatotype.

Method

With this in mind, twenty-one traits of psychological disturbance, assessed during the psychiatric interview with patients and controls, have been selected from a longer list. All these traits, except insomnia, which was assessed either present or absent, were estimated on a 7 point scale, 7 indicating greatest severity, 1 absence of the trait.

In defining these traits, psychiatric jargon has been avoided. Nevertheless, the 21 traits appear to embrace the commoner adolescent syndromes of affective

disturbance with anxiety or depression, obsessionalism, hysteria, inadequacy of personality and conflict with parents: together with possible prodromal signs of schizophrenia.

Findings

Table IX gives the percentage prevalence and ratios between patients and the controls series of insomnia and higher scores (5 plus) on the other 20 traits.

TABLE IX

Best Discriminating Characteristics from Clinical Interview

	Numbers Scoring High (5+) on 7 Point Scale		
	100 Patients	100 Controls	Ratios
1. Depression as judged by appearance and speech	29	0	29 : 0
2. Inability to concentrate	51	1	51 : 1
3. Easy fatiguability	22	1	22 : 1
4. Excessive demand for attention	22	1	22 : 1
5. Over dependence	35	2	17 : 1
6. Tendency to run away from difficulties	26	2	13 : 1
7. Self dramatization	39	3	13 : 1
8. Immaturity in general attitude to life	47	4	12 : 1
9. Inferiority feelings	32	3	11 : 1
10. Insomnia	41	4	10 : 1
11. Perfectionism	37	4	9 : 1
12. Narcissism	37	4	9 : 1
13. Insecurity	51	7	7 : 1
14. Distractibility	22	3	7 : 1
15. Indecisiveness	33	5	7 : 1
16. Irritability	19	3	6 : 1
17. Disturbed relationship with mother	41	7	6 : 1
18. Overanxiety	38	7	5 : 1
19. Excess preoccupation with specific topics	38	7	5 : 1
20. Excessive non-compulsive rumination of abstract topics—day dreams	25	5	5 : 1
21. Disturbed relationship with father	42	11	4 : 1

If one point is awarded for the presence at that level, of each of the 10 most discriminating traits shown above the line in Table IX, and if a total score of 2 constitutes abnormality, only 12 per cent. of both patients and controls are misclassified. These 10 traits at first sight appear to possess a discriminating power greater than that of the objective combination of somatotype and M.M.P.I. It must, however, be appreciated that much closer acquaintance was gained with the patients than could be obtained with the controls in an interview lasting one hour, and this bias may partly account for the better discrimination afforded by the psychiatric traits selected. This brief method of interview is, therefore, but tentatively propounded as a first rational step towards the development of a psychiatric scale of student vulnerability: its efficiency in the field is as yet untested.

SUMMARY

1. Mental upset continues to be the leading cause of prolonged absence and illness among Oxford students.

2. The problem has been studied at a local N.H.S. centre for acute psychiatric illness by examining 100 consecutive student patients referred by their general practitioners and 100 healthy volunteers.

3. Examination was by somatotype, electroencephalography, clinical psychological tests and psychiatric interview.

4. A somatotypical bias among the 100 volunteers was shown by comparing them and the 100 patients with a sample of 405 pilot health service students.

(a) *Patients compared with pilot health service*

Among the patients, central endomorphs and central and peripheral endomorphic ectomorphs were significantly more common. Endomorphic mesomorphs and central mesomorphic ectomorphs, were significantly more common in the health service sample.

(b) *Volunteer controls as compared with pilot health service*

Among volunteer controls, mesopenes, particularly endomorphic ones, appeared significantly more frequently; mesomorphs attended significantly more often in the health service sample.

5. There is evidence that findings differentiating patients from controls would be likely to differentiate patients still more strongly from the University at large.

6. Differentiating factors between patients and controls of varying significance are discussed.

(a) *Social Class*

No significant difference was observed in respect of social class, financial security, national service, broken homes or religious interest changing in the first year of residence.

(b) *EEG*

No significant difference was observed in the prevalence of electroencephalographic abnormality.

(c) *Intelligence*

(i) *A.H.5 Test.* There was no significant difference in Part I (verbal) between patients and controls. In Part II a small but significant number of patients obtained lower scores (Grade D and E) than controls, but there was no significant difference in the upper three grades (A, B and C) of Part II.

(ii) *Honours Class.* Patients taking final honour schools obtained percentages of first, second, third and fourth class honours comparable with the University at large in 1953.

(iii) Neither high nor low intelligence can therefore be regarded as an important factor in producing psychological breakdown.

(d) *Previous and Family History*

Significant but possibly biassed differences between patients and controls were found in the spheres of previous psychological illness, psychological illness among relatives, disharmony between parents and disturbance of relations between the subject and members of his family. None of these differences was of a high order.

7. *The Establishment of a vulnerability scale.*

(*a*) The Minnesota Multiphasic Personality Inventory differentiated all but 31 per cent. of patients from controls, taking as abnormal a score of 70 obtained on any one scale.

(*b*) If the optimum M.M.P.I. score shown to differentiate patients from controls in separate somatotype areas is used in conjunction with the somatotype, only 19 per cent. are misclassified.

(*c*) Although the results may be biassed, if the 10 traits of psychological deviation found at psychiatric interview to differentiate most satisfactorily between patients and controls are used, misclassification is further reduced to 12 per cent.

(*d*) In practice this heuristic vulnerability scale could be used by submitting students to somatotyping and M.M.P.I. testing on entry, and those with "vulnerable" results to a 15 minute psychiatric interview designed to elicit the 10 discriminating traits.

(*e*) This procedure would occupy about 2½ hours of each student's time. It might be employed either as an aid to early diagnosis, or for routine screening after university entry.

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WITCHCRAFT AS A PRIMITIVE INTERPRETATION OF MENTAL DISORDER

By

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Preface

The following facts concerning West African witchcraft were observed and recorded by the present writer while working as an ethnologist in the Gold Coast. The writer had not, at that time, any psychiatric experience, but has since worked in British mental hospitals long enough for the facts to invest themselves with psychiatric significance.

West African Ideology of Witchcraft

Gold Coast witches, in contemporary African belief, are associated with a secret religious cult of their own. No such cult in fact exists, but the belief in its existence is probably based on fact and represents a garbled fragmentary tradition of a pre-agricultural religion, long superseded. It is believed that companies of witches, under a group-leader, hold secret nocturnal meetings in inaccessible places and travel to these gatherings by flying through the air or by riding on antelopes, leopards and owls. These meetings are cannibalistic feasts: the bodies of the witches' victims are cut up, cooked in a pot and eaten. The rank of a witch in the company determines whether he or she shall receive the head, the trunk, the hands and so on.

The fact that a witch has been demonstrably asleep on her mat throughout the night which she is supposed to have spent in feasting, and the fact that the corpse of the victim, slain supposedly by witchcraft, has clearly suffered no cannibalistic ravages, are covered by African dogma. It is the spirit (*susuma*) of the witch that leaves her sleeping body and flies to the meeting-place. It is not the victim's material body, but his vital *kla* which is eaten by the witches.

The *kla* is usually pictured as an invisible double and is the essence of physical life. Though a person's *susuma* may leave his body in dreams or in mind-wandering without ill effects, the *kla* cannot leave without causing sickness and death. If the witches steal away a man's *kla* and cut it up, he becomes mortally sick. If they then relent, re-assemble the parts and restore them to him, he recovers. If, however, they have already eaten, say a leg, and hence cannot restore it, he recovers except for a permanently useless leg. If the witches steal only that part of the victim's *kla* corresponding to the womb or the penis, the victim becomes either barren or impotent.

Besides causing illness, death and sterility, witches are also believed to blight crops and to cause accidents, financial disasters and ill-luck.

Witchcraft must not be confused with other supernatural and evil ways of causing trouble and death. Curses, charms, prayers and sorcery all have their place, but they involve ritual acts and sometimes concrete apparatus. The distinguishing feature of witchcraft is that it is wrought solely by the silent invisible projection of influence from the witch. Furthermore, she has no conceivable

motive. She kills and injures, not those to whom it would be natural to wish harm or death, but those in whose well-being she may even have an interest. This is incomprehensible and therefore sinister. No one is surprised to find wickedness among wicked people, but to find it professed by hitherto good and kindly people is mystifying and appalling.

All this, however, is simply part of the body of African theory of witchcraft. What keeps the whole activity alive are the people who claim to be associated with it.

Activity of and Response to Gold Coast Witchcraft Today

Before attempting to describe any of those mentally disordered people who are the sustenance of Gold Coast witchcraft, it should be said that during the years 1920–1944 (and for aught I know during the past ten years as well) there was in the forest-country an enormous increase in preoccupation with witchcraft. This is attributable, firstly, to the sterility resulting from widespread gonorrhoea; secondly, to the almost universal poor nutrition and physical indisposition; thirdly, to the cocoa and mining industries which have in innumerable ways disturbed the even tenor of domestic and marital life; and fourthly, to the spread of literacy and literate occupations with consequent conflicting standards of behaviour, new insecurities and resulting neuroses.

Though we are not concerned here with the ecology of present-day witchcraft in the Gold Coast, it is interesting in the light of Hare's work on the ecology of mental disorder in Britain (1). Among the dwellers on the Gold Coast coastal plains, the Akwapim peoples, the Adangme peoples and the Northern territory tribes, who are all better fed, less diseased, more vigorous, more prolific and more cheerful than the forest peoples, witchcraft is comparatively rare. It is interesting also to compare Gold Coast witchcraft with that of the Trobriand Islands (2). Though the dogma of witchcraft is strikingly similar —the night-flying, the eating of the invisible double and so on—the Trobriand Islanders are a singularly happy, healthy people and the whole atmosphere of the topic is relatively light-hearted.

To meet the new preoccupation with witchcraft in the Gold Coast forest-country, innumerable shrines of a completely new kind have been set up. Each of these is in charge of either a single owner who works as a private practitioner, or of an elder appointed by the community which, by public subscription, bought the shrine. The private practitioners' shrines are the more interesting, for they are often in remote parts of the forest and are virtually native mental hospitals dealing with both out-patients and long-term voluntary in-patients.

The practitioner, though his explanations are provided by his theory of witchcraft, is frequently a psychotherapist of no mean order, and his results are such as our own psychiatrists might well envy. Nearly every day a party of clients come to see him bringing their witchcraft problem in the shape of what would in this country be regarded as a patient. These patients fall into several distinct categories:

(1) The confessed witches, moaning of the evil they have wrought. These are depressives and it is their own affirmation of guilt and unworthiness that initiates the proceedings.

(2) People complaining that witches have stricken them with such ills as sterility, blindness, excessive bereavement and misadventure. These regard themselves as suffering from what I shall call simple bewitchment. They seldom seem to be neurotic.

(3) Terrified, anxiety-ridden people, who, though protesting that they have never yet done any harm, feel themselves being converted into witches against their will. I shall call their plight malignant bewitchment.

(4) Healthy people who seek, in return for a very moderate fee, to receive supernatural immunization against besetting evils.

The practitioner conducts the first hearing of any case ceremonially before his shrine. The accompanying ritual need not concern us here, except in its function of enhancing prestige, strengthening suggestion, and fortifying reassurance. He then most thoroughly investigates the family history and the stresses to which the suppliant is subjected. He ferrets out the envies, spites, rivalries, marital troubles, kinship disputes and temperamental clashes. Ruthlessly he lays bare everyone's secrets. Astonishing tales of guilt and misdemeanour often emerge. Then he sums up the situation as he sees it—and as the suppliants have now to see it. He announces who should confess and apologize and to whom. He admonishes, he advises, he knocks heads together. He cleanses, he reassures.

Sometimes he keeps a suppliant for a long stay of treatment in his forest compound, giving daily psychotherapy, daily ritual at the shrine, good food and a change of scene. Between him and the suppliant springs up a striking transference situation which he handles with masterly skill, referring his own influence over the suppliant back to the deity of the shrine, to whose permanent protection he is now commended.

Healthy people, seeking immunity from witchcraft, take ritual drinks before the shrine. On these people the practitioner impresses the indubitably sound doctrine that it is futile for any man to expect health and prosperity if there is rankling in his heart secret spite and resentment towards any fellow-man, and he takes appropriate steps to ensure that the suppliant cleanses his mind of any such rancour.

The Witches

When the abject witch tells her self-abasing tale before the shrine, it is noticeable how often there is a history of bereavement, sickness and worry ushering in her conviction of sin.

One witch said, "When my mother was dying I sat behind her and held her and gave her water and she breathed her witchcraft into me with her last breaths. I was ill for some time then without knowing the cause but after a few moons I became certain that I was a witch."

Another said, "I inherited everything that belonged to my dead sister and as she was a witch I inherited that too." Inheritance in the Gold Coast means mainly the inheritance of obligations, and among women such responsibilities as the care of children.

Another witch said that her dead mother sent the power of witchcraft upon her because she was discontented with the inheritance this parent had left her.

Yet another witch said of her evil genius, "It was given me by my brother. He told me that my daughter had got him into debt and that some day he would make me suffer for it. I didn't know at the time that he was going to make me a witch."

Especially is it noticeable that the loss of children is a frequent feature in the history of self-confessed witches.

One said, "Seven of my children are dead: one remains alive . . . The members of our company have to make contributions in turn. When my turn came round from time to time I brought them to be killed by my company."

Another declared, "I have borne seven children. Four of them are dead. I killed them . . . I have lately killed one grandchild." Observe that this woman is now at the age of grandparenthood.

Yet another affirmation ran, "I have borne ten children. Five are alive. I killed the others myself."

And yet another, "I have killed seven children of my own, and eaten them with my company."

Another typical witch asserted, "I have killed five of my own children and my grandson."

And yet again, "I have killed three of my own children and seven of my kinsmen's children."

One witch who seemed unusually disposed to set a limit to her self-reproach said, "I have given to my company my own six children and no more."

Another asserted, "I have put a sickness into my brother's belly and into that of his wife so that they shall have no more children . . . When they get any money I cause them to lose it and thus I keep them in want."

Notice also that the depressive conviction of sin is apt to crystallize out of a matrix of family strife as well as family misfortune.

One witch averred, "I and my company have killed many and spoiled everything. We spoiled people's tempers in our family."

Concerning kinship tensions, it has long been fashionable among anthropologists to dismiss witchcraft as a mere expression of such tensions (3), and to perceive blame being fixed where envy and spite would naturally fix it. This view can seldom be taken of Gold Coast witchcraft. The background of family strife is certainly often there and contributes to neurosis, but the blame is claimed in no uncertain terms by the last person on whom anyone would conceive of fixing it.

Other witches present a more "mixed picture" than that of the classical depressive, but we still observe that it is the witch herself who voluntarily comes forward with her load of self-blame. The picture always contains a "depressive element". Whether there is ever present an additional element of obsessive fear, I have not enough information to know.

The following two cases I witnessed while staying in a village which possessed a publicly-owned shrine.

Case 1

Affua O., a woman in the later child-bearing age-group (no illiterate African knows his own age), gradually became more and more ailing and upset. She became deaf, then she became unable to stand. At length she called her mother and confessed that she was a witch. She said she had caused thirteen deaths among her own kinsmen, and five among her husband's, and was planning to kill him also. She belonged, she said, to a company whose meeting-place was far away and her spirit was in the habit of travelling there in a big motorcar—a new variant of the flying dream and the animal-riding dream. She it was, she said, who had caused an elder's wife to have a long and difficult labour, not in order to injure the wife, but to make the husband call in expensive medicine-men and so become impoverished. It was she, she declared, who was "holding the wombs" of all the barren women in the district. She had offered—in the spirit, without physical communication—to sell her own child's leg to another witch. The offer was refused and the leg remained well, but, had it been accepted, material money would have come to the seller as an apparent windfall, and when the purchaser invisibly removed the spiritual counterpart (*kla*) of the leg, the child would have lost the use of his material limb. The self-accused woman was further planning, she said, that her husband should be killed by a log while helping to load a timber-lorry. The husband, however, had drunk protective medicine at the shrine, so the medicine had turned up on the plotting wife on the eve of the day she had marked for his death, had made her mortally ill and forced her to confess.

She was forthwith carried—being unable to walk—to the shrine. There she repeated her confession and added that she was on bad terms with her husband, who kept her short of money and clothing. She said she had been born a witch and that the seat of her daemon was in her head. The elder in charge of the shrine said that, this being so, she could be only partially cleansed, though her power to do harm could be removed.

She was then required to perform the ritual of beheading a fowl before the shrine. The

fowl, dying breast downwards instead of breast upwards, indicated that her confession was incomplete. Thereupon she added that her own baby gave her no pleasure at all as it cried without ceasing, so she had been planning to kill it by witchcraft. She then beheaded another fowl, which died in the manner indicating complete confession. She immediately recovered her power of walking and walked home.

Case 2

Ama G., again exhibits a "mixed picture". Her witchcraft history began shortly after the death of her two-months-old child, when she fell ill and said that it was she who had killed, not only this child, but four earlier ones. She asked to be taken to the shrine to complete her confession and be cleansed.

At the shrine she said that her daemon abode under her eyelids in the form of a centipede. She said that she had a secret song that she silently sang to it. When she sang, her daemon became active and did destructive deeds. It had killed her own five children, her sister's four children, and her sister.

At this point in her public confession she grew highly excited and sang her song aloud to the assembled populace. She then said that her parents, her brothers and her sisters were in poverty and that this was her fault.

She also said that she had transformed the main street of the village into an invisible river and that everyone who crossed it lost threepence for each crossing, with the result that everyone in the town remained poor.

She further said that it was she who had prevented the European diamond-mining industry from coming to the village and enriching it, for she had, in spirit, dug up all the diamonds and hidden them in the river. She had also taken away the resolution of those who would otherwise have started the diamond industry.

She added that her husband had never pleased her and that once, years before she became a witch, she had ritually cursed him.

After a few more confessions she was fined one goat, which was sacrificed before the shrine.

The principal outcome of the incident was that her husband divorced her, an event they had both long desired, and which, when accomplished, made them both happier.

Simple Bewitchment

The people who on account of gratuitous misfortune look around for witches to blame are relatively few. So long as people are mentally stable, they suffer grievous disasters without complaint. Even children's deaths are borne with fatalistic fortitude, a cruelly high infant mortality rate having for centuries seemed inevitable. It is mainly in retrospect, at the age of involutional melancholia, that the witch looks back and feels that she has killed her children.

One man, deemed to be a victim of simple bewitchment, was a literate schizophrenic whom I saw undergoing treatment (not at one of the new shrines but by a long-established old leech). He was regarded as afflicted and mad—for which latter term I believe every language has a word and every culture a concept. He was pitied, not persecuted, just as a blind man would be. No frenzied hunt for the author of his ills, so far as I know, had been instituted, for it was held natural that he, a literate, should have malicious enemies. His wife and his mother were together looking after him and they too were objects of neighbourly compassion. But they were looking worn and worried, and should his mother have thrown, as well she might, a reactive depression and announced herself the cause of his plight, this unnatural avowal would have brought the hornet's nest about her head.

A common example of simple bewitchment which raises no hue and cry is that of the schoolboy who has failed in his examinations, and complains that illiterate relatives, envious of his advance in life, have by witchcraft spoilt his brain.

Another man who had lost, through death, several wives and nineteen children, shrugged and said resignedly that he supposed it was the work of some witch. He made no attempt to pursue the matter further.

Again, a man who suffered agonizing jumping pains in his head at night attributed them to witches' use of his head as a football at their nightly revels.

On the whole, people with whom fate has dealt very harshly accept their lot philosophically and seldom is witchcraft invoked to explain it.

Malignant Bewitchment

Far more common, and far more interesting, than the people who feel themselves bewitched are those who believe that the power of witchcraft is being thrust upon them. Witches can do worse than killing and injuring: they can turn other people into witches like themselves, no matter how unwilling the recipient of the evil power may be to possess it. And when frightened people begin to think that witches are after them they think of them as doing their worst. They seldom claim to be simply bewitched.

In this group again there is ample room for an obsessive element but I have not as yet any firm evidence of its existence.

Many of these people are first led to suspect themselves of being incipient witches by seeing "witches' fire" in front of their eyes—flashing lights and sparks which, from their descriptions, may well be the fortification spectra of migraine. Others feel frogs, snakes and worms crawling inside their bodies and limbs, particularly in their throats.

Case 3

Kofi A., a farmer, was received into a practitioner's compound for long-term treatment. When I first saw him, he was miserably thin, terrified and haggard. His malady began, he said, with sleeplessness, short intervals of unrestful sleep being filled with nightmares during which his *susuma* was drawn unwillingly away to join a band of witches. He developed daily periods of blindness and became unable to hear anything except the urging voices of the witches. He also had abdominal pains and his belly was scarred where he had made cuts to let out the evil. He consulted one leech after another and in despair even travelled to a coastal town and saw a European-trained doctor, who could find nothing wrong.

After a few weeks in the practitioner's compound with appropriate ritual and psychotherapy, he recovered his sight and normal hearing, though he was still languid and spent, sitting about on the ground, afraid to go out of the practitioner's sight. But in his presence he felt a sense of safety and the belief that he was to be rescued.

He stayed about a year and I saw him many times, gradually getting fatter, losing his hunted look and gaining the confidence to go out alone. At the end he was a different creature, with the normal African loquacity and sense of fun. He went home energetic and confident of his power to remain well.

Case 4

Kodzo S., a literate clerk and a long-term patient, said that his relatives had long been trying to destroy him and had finally decided to make him a witch. They first took away, he said, the use of his right hand, which made him a failure as a clerk. When I first saw him, the hand was, under the practitioner's treatment, improving, though it trembled severely, especially when he talked about it. He was a weak-looking personality with a quivering lower lip. He had been to many medicine-men and to one Government hospital. At the latter he was told that nothing was wrong with him, which strengthened his conviction that it was no natural power destroying him.

After a few months of native psychotherapy in the practitioner's peaceful compound, with nightly purifying baths before the shrine, the daemons were drawn out of him and he went home well.

It might well be supposed that the purposes of Kodzo S. would have been amply served had he merely lost the use of his writing hand through simple witchcraft. There was, however, no *belle indifférence* about him: he was terrified, and nothing short of malignant witchcraft satisfied him.

Case 5

Akua O., a young woman, felt herself being made against her will into a witch. An older woman came forward and confessed to be doing this. They were both brought to the shrine, where I saw them together. The girl was skeleton-thin and far too weak to walk. She had been ill for four years and had not walked for the last two, but she seemed alert and interested in the proceedings. After formal confession, the witch was purified and made to bless her victim, who was also bathed and purified. After this she was given a room in the practitioner's compound. Gradually she improved, put on flesh, learnt to walk again and to do her own cooking. She went home quite well and happy.

Witchcraft in Britain

It has been well established, mainly by the scholarly work of Murray (4), that the concept and ideology of witchcraft in Britain had its original basis in the survival of a pre-Christian religious cult of great—probably pre-agricultural —antiquity, practised as a persecuted, "underground" movement concurrently with Christianity.

But long after this movement had died out and secret meetings and rites had ceased, vague and fabulous ideas about the evil supernatural powers of witches continued to prevail. It became the custom, when cows aborted, swine took fever, crops failed, floods rose and people perished, to look around for a witch.

It has been a matter for much modern bewilderment that the guilt was almost always laid at the door of some lonely, poor and wretched old woman, hitherto submerged in humdrum insignificance.

The explanation suggested by the witchcraft of West Africa is that the old woman voluntarily asserted and insisted upon her guilt.

This is further supported by facts which confront us in the mental hospitals of Britain today. There is no more familiar figure in the admission wards than the agitated depressive, weighed down with extravagant and unshakable self-reproach.

Case 6

Mrs. H., a married woman of 69, was admitted to hospital with a six-months history of increasing depression, sleeplessness and loss of weight. She was in great distress but was rational and gave a moderately good account of herself. She said she could hear accusing voices telling her that she was not fit to live. She said of her mother, who had died 45 years earlier, "I think I broke her heart", and of her husband's poor health, "It is my fault. He has been a lovely husband and I have been a rotten wife." She said that for her misdeeds she would be hanged. She also declared that she had brought harm to the whole hospital.

She was treated with a short course of E.C.T. and made a dramatic and complete recovery.

Case 7

Mrs. B., a widow of 55, was admitted in an agitated depression. She was retarded, speaking slowly in a whisper. She covered her face, wrung her hands and moaned. The content of her speech was exclusively self-abasing. "I have brought destruction . . . I'm ashamed . . . I did it without thinking . . . I've defied the Lord . . . No one else has been so wicked as I have . . . Why should all these people have to suffer for me? I don't know how to put my head in the air at all . . . I'm not fit to speak to you . . . All the floods and all the war: it must be me to blame."

She was treated with a course of six E.C.T. shocks. After three she was able to smile, speak freely and help with the ward work, but when told that she would soon be well still replied, "I don't think so: I've done harm to so many people." After three more shocks, she had completely recovered and was discharged.

It needs but little imagination to picture the reception of such self-accusations three centuries ago.

Another probably relevant type of case which crops up sporadically in our own mental hospitals is that of the patient who believes that he or she can kill or harm others by means of an ill-defined influence. The picture differs from the depressive picture. The patient is predominantly alarmed, even panic-stricken. He does not claim to have done harm, but he feels that he could do harm and is terrified lest he should. I am not now referring to the obsessive-compulsive with his impulse to strangle or stab, or his delusion that he is spreading pestilence by means of his own ill-gotten germs. Such a patient postulates an acceptable mechanism of harming, a weapon, a material agent or a violent act. There is no implication of any mysterious means of destruction, though there is indeed a mysterious force which he feels to be impelling him.

Unlike the depressive, the patient afraid of his own potential destructive influence has enough insight to know that his belief is absurd. He may even have enough to suspect its relation to a guilty unacknowledged wish.

Case 8

Mrs. M., a married woman of 49, was admitted to hospital with a three-weeks history of anxiety and fear. The illness began when her mother-in-law fell ill of a paralytic stroke and it seemed likely that Mrs. M. would have to nurse her, possibly through years of helplessness. Mrs. M. harboured a wish that her mother-in-law would die. She felt guilty, not because of the wish itself, which could reasonably be regarded as a humane one, but because of her own disinclination to undertake the arduous nursing. She felt that the devil had put the wish into her head and she began to hear his voice. She began to feel that she had an influence over other people and could do them harm by making them do wrong things and make disastrous mistakes. Whenever she went to see her sick mother-in-law she felt that her bad influence was going to harm her. She felt no impulse to harm her directly. She became tormented and frightened by the devil's voice, which jibed, answered back her thoughts and taunted her, saying –"You've had it", meaning that she was going mad. She was soon weeping with fear and panic. The mother-in-law resolved the conflict by dying, whereupon Mrs. M. began to recover, and had, in fact, much improved by the time she entered hospital.

On admission she was correctly orientated, co-operative and pleasant, and she gave a clear, straightforward account of herself. Her hallucinations had almost died out and no longer distressed her. She was not noticeably depressed and recovered within a fortnight with no treatment beyond simple explanation and reassurance. Objectively, there was nothing wrong with her at any time except her distress at the subjective experiences which she clear-headedly described.

We have thus in our midst today at least two types of people who proclaim as a spontaneous unlearned response, unconditioned by—indeed flying in the face of—their encompassing culture, that they are the very stuff of witchcraft.

Summary

In parts of the Gold Coast today, neurosis is displayed, not only by depressed "witches", but by persons believing themselves bewitched.

An increase in neurosis, attributable to social and economic changes, has led to an increased preoccupation with witchcraft.

The untutored response of Gold Coast Africans to this neurosis includes a primitive but effective form of psychotherapy.

The affirmations of guilt that are a feature of severe depression suggest the postulate that many "witches" of Britain instigated their own punishment.

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THE VALUE AND LIMITATIONS OF CHLORPROMAZINE IN THE TREATMENT OF ANXIETY STATES

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Chlorpromazine hydrochloride (Largactil) introduced by Laborit (1952) has aroused considerable interest on account of its varied pharmacodynamic actions and clinical reports drawing attention to its possible use in anaesthesia, general medicine and psychiatry.

Chemically related to certain antihistamine drugs, it has little antihistaminic activity itself but has diverse effects on the nervous system. It is a neural depressant with central and peripheral action, vagolytic and sympatholytic properties. (Chauchard, 1952; Courvoisier, 1953; Sigwald and Boutier, 1953; Staehelin and Kielholz, 1953; Lehrman and Hanrahan, 1954; Anton-Stephens, 1954; Winkelman, 1954; Garmany, 1954; and Elkes and Elkes, 1954.)

Enthusiastic claims have been made regarding the therapeutic value of chlorpromazine in a wide variety of psychiatric disorders; many of these have failed to carry conviction, as most of the reports are based on mixed groups with an insufficient number of patients in each diagnostic category to justify definite conclusions and also because controlled procedures were rarely used.

We therefore decided to confine our investigation to one type of psychiatric disorder and chose anxiety states, since the reported pharmacodynamic actions of the drug suggested that it might be of value in the treatment of states of anxiety and tension. The total group studied consists of 150 patients all of whom are treated as out-patients.

Plan of Trial and Methods

In planning the therapeutic trial it was necessary:

(*a*) To ascertain the possible role played by suggestion, as distinct from the pharmacological properties of the drug, in achieving therapeutic effects.

(*b*) To take into account the possibility of improvement occurring during the trial period either spontaneously or due to factors unrelated to the pharmacological properties of the drug.

(*c*) To employ standardized detailed methods of recording clinical state and symptomatology so as to facilitate statistical comparison of changes during the trial period.

With these needs in mind the following methods were used:

(1) *Double Blind Method*

It was considered essential that neither patient nor physician recording clinical changes should know when active or inert tablets were being administered.

The inert tablets used were supplied by Messrs. May and Baker and were identical in size and appearance to the 25 mgm. Largactil tablets.

The inert and active tablets were marked X or Y for identification purposes by the dispenser, the only person knowing when active or inert tablets were being administered.

(2) *Sequence Control*

In order to control the possibility of any improvement due to factors other than the pharmacological properties of the drug and also to take into account the possibility of persistence of the pharmacological effects of chlorpromazine into the ensuing period of inert tablet administration, it was decided to give one half of the patients X tablets for the first part of the trial and Y tablets in the same dosage for an equal period afterwards and the other half of the group tablets given in reverse order.

(3) *Clinical Assessment*

For the purpose of uniformity of recording and to facilitate detailed comparison a special item sheet was devised for the investigation. The item sheet contained information regarding the social data, family and personal history, personality, clinical state and symptomatology. Particular attention was given to the recording and assessment of various aspects of emotional tension such as verbal reports of tension, bodily symptoms of tension, somatic signs of emotional tension, neuromuscular tension and autonomic lability which were rated on a seven-point scale according to severity. Finally a composite rating of total tension was made for each patient.

This method permitted ready detailed comparison of changes occurring during and after treatment.

Clinical assessments and ratings were made as follows:

(1) Before onset of "tablet" administration.
(2) After treatment with X tablets.
(3) After treatment with Y tablets.
(4) At weekly intervals thereafter.

Clinical Data

The series of 150 patients consisted of males 49 and females 101. The age distribution was as follows: 16–25, 12 per cent.; 26–35, 30 per cent; 36–46, 30 per cent.; 46–55, 16 per cent.; 56–65, 8 per cent.; 66–75, 4 per cent.

The patients were selected because anxiety and tension were predominant in the clinical picture. Under the diagnostic term "anxiety state" a variety of clinical syndromes are subsumed, depending on the patterns of somatic expressions of anxiety and tension and the presence of depressive, obsessional, hysterical or hypochondriacal features. The variety of symptoms occurring in the group enabled observations to be made on the effect of chlorpromazine on a number of mental and physical aspects of anxiety–tension states.

Dosage

The tablets used were Largactil 25 mgm. (May and Baker) and inert tablets of identical size and appearance.

During the period of the double blind trial the following tablet dosage was applied. On the first day, one tablet and increasing by one tablet daily until three a day which was continued for fourteen days. The same dosage was

applied for both X and Y tablets. This enabled a daily dosage of 75 mgm. of chlorpromazine to be given for two weeks. The total period of the blind trial was therefore 32 days.

After the blind trial period, continued treatment was given with chlorpromazine in order to determine optimum effects and to observe changes over a longer period. In these patients the dosage was gradually increased until optimum clinical effects were achieved or until evidence of drug saturation occurred such as dryness of the mouth and marked lethargy in the day time.

There was considerable individual variation in the optimum dosage. We found that in the majority of patients a daily dosage of 75–100 mgm. was adequate but some patients needed higher doses, e.g. 200–300 mgm. daily.

The optimum dose was continued for 3–4 weeks and then gradually reduced. If symptoms returned the dose was increased again for a further period before gradual reduction and termination.

Clinical Effects of Chlorpromazine

The clinical effects of chlorpromazine may be considered from the patients' subjective reports and by more objective evidence appertaining to clinical signs, the appearance and behaviour of the patients.

Subjective Reports

About three-quarters of the patients reported an improvement in symptoms and subjective state initially. The effects were usually relief of anxiety, tension and apprehension. There is a feeling of calmness without the dulling of alertness which often occurs with barbiturates. Patients describe the change as a natural feeling of ease and calmness.

There is a tendency for energy and drive to be decreased. If dosage is increased beyond the optimum, marked lethargy and even stupor may develop. In fact the dosage must be adjusted in each patient with the aim of relieving symptoms without producing an undesirable degree of inertia or lethargy.

The reduction in anxiety, tension and apprehension is usually accompanied by increased confidence and a number of our patients who previously, on account of their anxiety states, had been unable to venture out of their homes on their own were now able to go out alone, visit places of entertainment and travel on public transport, etc.

Appearance and Behaviour

The beneficial changes with chlorpromazine therapy are sometimes apparent in the patient's appearance, clinical state and general behaviour even before he recognizes or reports improvement.

The tense, strained appearance of the anxious patient is replaced by a more relaxed and contented countenance. General attitude and posture more relaxed. Relatives and friends may notice that the patient is not so readily upset by the stimuli or situations which previously evoked undue emotional reactions.

Although problems and conflicts may still be present, the patient states that they do not trouble him so much as previously. Patients who during their illness were too anxious or preoccupied to read newspapers or books, listen to the radio or watch television became more interested and participated in these activities with greater enjoyment. Appetite, when impaired by anxiety and tension, improved during chlorpromazine therapy.

Symptomatic Effects

Comparison of ratings of symptoms and signs before, during and after chlorpromazine therapy revealed that some clinical features were more frequently alleviated than others.

(a) *Clinical features most frequently alleviated*

Symptoms which showed the most favourable response included general tension, anxiety and apprehension together with such bodily symptoms and signs as internal tremulousness, tremors, bowel frequency and urgency, stammering on excitement, excessive sweating and neuromuscular tension with its various symptomatic manifestations improved *pari passu* with improvement in general tension and anxiety.

(b) *Symptoms showing variable response*

Certain symptoms showed a variable tendency to improve.

Insomnia for example was improved in 50 per cent. of patients, in 40 per cent. it was not changed and in 10 per cent. it became worse. A similar distribution of therapeutic effects applied to palpitations, 45 per cent. being improved, 40 per cent. not improved and 15 per cent. made worse. Headaches were only improved in 35 per cent., 50 per cent. were not improved and in 15 per cent. the headaches became more severe. Only half of 10 patients with severe vomiting as a predominating symptom were relieved by chlorpromazine.

(c) *Symptoms showing little tendency to respond*

Postural dizziness and fainting showed little tendency to improve and in some patients developed as a new symptom with chlorpromazine. Premenstrual tension symptoms as a rule were not significantly relieved with chlorpromazine.

We were not able to confirm the claims of other authors that chlorpromazine given alone was particularly helpful in relieving pains, whether predominantly psychogenic or physiogenic in origin.

Side Effects

The following side effects and complications occurred:

(1) Dryness of the mouth occurred in most patients if the dose were increased beyond optimum.

(2) Constipation was common in early stages of drug administration but passed off without special treatment.

(3) Tachycardia and palpitations were in some patients so disturbing that treatment had to be terminated.

(4) Postural dizziness, as might be expected from the hypotensive nature of the drug, tended to occur in early stages and usually passed off after a few days. If troublesome, patients were advised to lie down for half an hour after taking the tablets. We did not consider it advisable to give this advice to all patients, as the majority did not develop this symptom and we wished to avoid drawing the patient's attention unnecessarily to the possible development of this side effect.

(5) Pyrexia of 101–103° F. in three patients.

(6) Erythematous rashes in three patients, which after drug withdrawal cleared during the course of a week or so.

No patient in our series developed jaundice, a complication which has been reported by a number of authors.

Method of Grading Results

From the findings in clinical examination, interview ratings and assessments the results were graded as follows:

Grade		Weighting
I	Marked clinical improvement	+3
II	Moderate clinical improvement	+2
III	Slight clinical improvement	+1
IV	No improvement	0
V	Slight exacerbation of symptoms	−1
VI	Moderate exacerbation of symptoms	−2
VII	Marked exacerbation of symptoms	−3

By applying weights to the different grades it is possible to make allowance for any effects obtained during the course of inert tablets.

Thus if a patient had slight improvement with inert tablets (i.e. Grade III=+1) and marked improvement (Grade I=+3) with chlorpromazine, the degree of improvement attributable to chlorpromazine would be expressed by the difference between the weighting of the respective grades, viz. +2.

Results

The results will be described in two parts:

(*a*) The results during the double blind trial.

(*b*) The results obtained by treatment over a longer period.

Double Blind Trial

The gradings obtained in the double blind trial on 150 patients were as follows:

Grade	Chlorpromazine Per cent.	Inert Tablets Per cent.
I	10	0
II	34	2
III	22	8
IV	26	84
V	4	2
VI	4	4
VII	0	0

The difference between percentage improved with chlorpromazine (66 per cent.) and inert tablets (10 per cent.) is of high statistical significance (critical ratio over 12).

The fifteen patients who improved during the period of inert tablet administration had the following gradings with chlorpromazine. Six patients who had slight improvement (Grade III) with inert tablets showed no additional improvement with chlorpromazine. Six patients who had slight improvement with inert tablets (Grade III=+1) had marked improvement with chlorpromazine (Grade I=+3). The effect attributable to chlorpromazine in the latter group is therefore +2 for each patient. Three patients who showed moderate improvement (Grade II) with inert tablets became considerably worse with chlorpromazine (Grades V and VI).

Results obtained with chlorpromazine given over a longer period

The following were the results obtained by continued trial with chlorpromazine:

Grade	Per cent.
I	16
II	38
III	24
IV	14
V	4
VI	4
VII	0

The above results represent the best achieved in the series with Chlorpromazine. They must not be regarded as the final assessment as we found the relapse rate after initial improvement to be quite substantial.

Relapses

The following relapses occurred despite continued administration with chlorpromazine:

Of 24 Grade I patients 15 relapsed
57 Grade II patients 39 relapsed
36 Grade III patients 24 relapsed

Relapses occurred after periods varying from 2–10 weeks of improvement.

Results on Follow-up

The position at 3–7 months follow-up taking into account relapses was as follows:

Grade	Per cent.
I	6
II	12
III	8

Thus only 26 per cent. of the total group derived continued therapeutic benefit from chlorpromazine therapy and only in 6 per cent. did the effect amount to marked clinical improvement.

Discussion

The complexity of psychiatric material and the multiplicity of factors which may influence the course of a psychiatric illness make the scientific evaluation of new therapeutic agents difficult.

The utilization of controls is indispensable, but the choice of controls sometimes offers practical difficulties. Thus, the method of paired controls has inherent difficulties in psychiatry as accurate matching of patients with similar prognosis may be extremely difficult or sometimes impossible to achieve. The method of using the patient as his own control has much to recommend it especially if such methods as the double blind and sequence control procedures are utilized enabling the effect of suggestion to be ascertained and also the control of factors unrelated to the pharmacological effects of the drug.

Using these methods our results indicate that chlorpromazine has significant clinical effects attributable to its pharmacological properties.

Not all patients however were significantly improved; in fact the best results obtained even with extended trial at optimum dosages were 54 per cent. showing marked or moderate improvement and of these 66 per cent. relapsed

despite continued medication with chlorpromazine. Even in this group only certain symptoms were ameliorated. These facts indicate considerable therapeutic limitations of the drug even in anxiety tension states which some authors regard as being pre-eminently suitable for chlorpromazine therapy. Furthermore, in spite of the detailed methods used, we were unable to find precise indicators in clinical symptomatology which enabled an accurate forecast to be made indicating which patients are going to respond favourably. Clinically similar cases may show a markedly different therapeutic response to the drug. It was easier to forecast which patients are unlikely to respond favourably. Patients who were very inhibited, easily fatigued and markedly lacking in energy and initiative were not, as a rule, helped by chlorpromazine.

The occurrence of disturbing side effects is a further disadvantage, and patients should not be allowed to be in charge of machinery or vehicles until their reaction to the drug and development of possible side effects is known.

These considerations indicate the considerable limitations of the value of chlorpromazine in anxiety states and its main usefulness would appear to be for short term symptomatic treatment and management.

Summary

1. A controlled therapeutic trial of chlorpromazine in a group of 150 patients with anxiety states is described.

2. Utilizing the double blind method and other controlled procedures it was found that the results obtained by chlorpromazine were significantly better than with inert tablets.

3. Extended trial with chlorpromazine at optimum dosages resulted in 54 per cent. of the group showing marked or moderate symptomatic improvement. Two-thirds of these patients relapsed after a few weeks of clinical improvement despite continued medication with chlorpromazine.

4. This high tendency to relapse together with the development of side effects considerably limits the value of the drug. The usefulness of Chlorpromazine in anxiety states would appear to be largely restricted to short term symptomatic treatment and management.

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THE SIGNIFICANCE OF ABSTRACT AND CONCRETE BEHAVIOUR IN ELDERLY PSYCHIATRIC PATIENTS AND CONTROL SUBJECTS

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A—Introduction

The recognition of a well-established psychosis due to arteriosclerotic or senile brain changes rarely presents any difficulty. However, increasing numbers of elderly people are seen with affective, paranoid, or neurotic manifestations, and it is sometimes very difficult to decide whether their symptoms present prodromata of an organic psychosis, or whether in the absence of degenerative brain disease they are occasioned by a variety of endogenous and environmental causes leading to a "functional" psychiatric illness.

Possibly the importance of mild or early dementia when assessing a patient's illness has in the past been overstressed, since depressive illness in the aged is sometimes associated with intellectual impairment of a pattern closely resembling that of dementia, with complete restitution following recovery from the affective disorder (Lange, 1928; Madden *et al.*, 1952); on the other hand, the presence of signs of impairment such as memory defects and habit deterioration need not affect the response to E.C.T. of severely depressed and agitated patients (Mayer-Gross, 1945). But the outlook for lasting recovery from a mental breakdown seems so much better where there is no dementing process at work that the clinician continues to examine his elderly patients carefully for evidence of irreversible intellectual impairment or personality deterioration.

A summary of the literature on testing for intellectual impairment in elderly patients suggests the following conclusions: (1) Dementia which is clinically clearcut, or confined to a specific diagnosis such as arteriosclerotic or senile dementia, is revealed in a low I.Q. in intelligence tests, and in quotients indicative of deterioration such as the Babcock Efficiency Index (Botwinick and Birren, 1951), (2) Where the impairment is not of a gross kind, or when the tests are used to compare patients within an already restricted range of disorders, the impairment is not revealed by the I.Q., nor by ratios comparing verbal with non-verbal tests (Hall, 1952; Pinkerton and Kelly, 1952). It has been claimed, however, that tests based on the concept of abstract thinking (Hall, 1952) and those taking into account the reasoning used by the patient in reaching the right or wrong answer (Pinkerton and Kelly, 1952), demonstrate an impairment which is not revealed by the usual quantitative methods.

The work of Goldstein and Scheerer on brain-injured patients led them to make a distinction between two attitudes, the abstract and concrete, which they describe as "capacity levels of the total personality" (Goldstein and Scheerer, 1941). They suggest that in pathological brain functioning, "test results can be evaluated only by analysing the *procedure* by which the patient has arrived at his results" (p. 17). They present modifications of tests already in use, such as the Colour-Form Sorting test and the Kohs Blocks test, which enable such an analysis to be made, and suggest that while the normal person is capable of assuming both the concrete and abstract attitudes, the abnormal individual is limited to the concrete approach. "If this be true, tests that permit us to rate the performance of a patient according to this line of demarcation would have a diagnostic value of practical and theoretical import" (p. 30).

Although the exposition in their Manual implies that failure or success in assuming the abstract attitude on these tests is dependent on whether cerebral functioning is normal or abnormal, there is in fact little published information about the performance of normal or abnormal persons on the tests in the modified form adopted by Goldstein and Scheerer. It is generally implied that failure to perform the tests at an abstract level occurs primarily in patients with brain damage or disease and in certain schizophrenics. Bolles (1937) found that eight year old children of normal intelligence were capable of dealing abstractly with the test material. In an analysis of a number of psychological tests used for the evaluation of brain injury, Armitage (1946) reports the performance of 45 control subjects on, among others, the Goldstein-Scheerer Cube Test. Half of the controls were, in fact, psychiatric patients suffering from mild affective disorders, but all controls, of whom 12 were older than 35, solved the test problems at once or after only one or two auxiliary procedures to induce an abstract attitude had been given, though 15 per cent. were described as of only dull normal intelligence. Weigl's Colour-Form Sorting Test in its original form and without experimental variations was used in patients with well localized brain lesions by McFie and Piercy (1952), who found that even in this form the test was too simple, as only about 50 per cent. of the cases with dominant hemisphere lesions were unable to pass it. Most of their 74 subjects were over 40, the oldest being 66, and only 4 were described as of below average intelligence. Cleveland and Dysinger (1944) reported a striking degree of concreteness using the object-sorting test in senile psychotics.

B—Method of Present Investigation

The impression has been gained that the Goldstein tests are being used in many neuropsychiatric centres for the diagnosis of "early dementia", and it was felt that the geriatric unit of this hospital might be especially suitable for testing their usefulness, because to it are admitted elderly patients of a type likely to respond favourably to psychotherapeutic, social or physical measures; at the same time, some of these patients show definite, others only dubious, evidence for the presence of organic brain disease or degeneration, and it is desirable to discover a reliable measure of the degree and type of organic impairment.

A preliminary investigation with this aim in mind was reported by the authors to the Second International Gerontological Congress in 1951. The tests used included the Colour-Form, Cube, and Colour Sorting Tests, and the main conclusion was that none of these 3 tests discriminated between patients grouped by the psychiatrists according to the amount of organic involvement. This was

largely on account of the striking concreteness of most patients: only one of forty-nine had been able to perform all three tests at an abstract level, though fifteen patients had been judged clinically to be entirely free from psycho-organic features. This finding led to the examination of 2 control groups, one of young and one of elderly normal people, and the remainder of this paper will give an account of the investigation of abstract and concrete behaviour in elderly psychiatric patients, in elderly people without mental abnormalities, and in young "normal" adults.

(1) *Description of the three groups.* The patient group (A) consisted of 32 men and 17 women ranging between the ages of 60 and 84 years (mean age 68·88). Most of them exhibited affective disturbances, some with neurotic or paranoid colouring, but schizophrenics and paraphrenics were excluded. Though in most cases the clinical picture was of a psychotic degree of severity, only a few patients of the unit had to be excluded from this study because they were too severely disturbed to co-operate in the psychological examination; at the time of testing, no patient had received convulsive therapy during the present illness.

The control group (B) of old people free from psychiatric disorders consisted also of 32 men and 17 women ranging between the ages of 60 and 87 (mean age: 68·71). They were in- or out-patients of two neighbouring hospitals suffering largely from arthritic conditions or convalescing from cardiac or respiratory disorders; they present the final selection of a larger number of patients thought to be free from emotional or intellectual disorder by the doctors and nurses in charge; many had been rejected (by F.P.) as on administering a simple questionnaire of orientation, recent memory, and information, a suspicion of senile intellectual deterioration had arisen; others were found to be suffering from emotional disturbances, and three subjects refused to co-operate, though the purpose of the examination was frankly and fully explained to everybody. This control group (B) then was thought to be free from mental disorder, or deterioration other than from age, and had been matched for sex and age (within quinquennial groups) with the elderly psychiatric patients; both groups were similar in socio-economic structure, most members belonging to the skilled working class.

The young control group (C) consisted of 26 men and 20 women ranging between 15 and 39 (mean age: 26·85). They were members of the administrative and domestic staffs of this hospital, who had been approached as a group with a request for help in this piece of research; only two people refused or evaded testing. As otherwise all employees under 40 in certain departments were tested, there was no selection bias due to volunteering; on the other hand, this group was not matched with the other groups in sex composition and contained a larger proportion of unskilled workers with an associated lower intelligence.

(2) *Method of Testing.* The psychiatric group (A) was tested with the Raven Progressive Matrices (1950) and the Synonyms Section of the Mill Hill Vocabulary Test (1950) by the junior doctors in charge. The Goldstein-Scheerer Cube Test, the Gelb-Goldstein Colour Sorting Test, and the Weigl-Goldstein-Scheerer Colour-Form Sorting Test (1949) were administered by B.H. The two control groups were only examined with the Synonyms Section of the Vocabulary Test, the Cube Test and the Colour-Form Test, as it was thought wise to limit testing to one brief session of from 20 to 45 minutes. The B–group was tested by F.P. The C–group was kindly tested for us by Miss B. Loefving, while engaged on another project financed by a research grant from the Board of Governors of this hospital. The directions and criteria laid down by Goldstein

and Scheerer in their Monograph (1941) were strictly followed, and the three testers were able to reduce any possible differences of method or interpretation by personal discussion. They deviated from Goldstein and Scheerer only in not persisting with the Cube Test after the subject had been failing to assume the abstract attitude in more than two designs, as for obvious reasons they did not wish to produce catastrophe reactions in patients or controls.

(3) *Method of Scoring Tests.* Goldstein and Scheerer point out that any quantitative scoring should be based on qualitative observations and they specifically disclaim the possibility at the present time of elaborating "a definite scale of tests graded according to a more or less concrete and more or less abstract attitude involved" (p. 30). Performance on the Colour-Form and Cube Tests was therefore graded as either "abstract" or "concrete". "Abstract" performance on the Colour-Form Test was that in which the subject was able to sort the pieces both for colour and shape, without patterning, and to shift from one category to the other, regardless of whether he was successful immediately the material was presented, or whether he needed to learn from the various helping procedures. "Abstract" performance on the Cube Test was that in which all the designs were correctly reproduced from the small, unlined design, either when this was first given or after the patient had succeeded in correctly reproducing the design at any of the later stages.

C—Results and Evaluation

(a) *Psychiatric Group (A):* The subjects were placed in the following three categories by the two psychiatrists working with the cases on the basis of history, physical examination, and mental state, which included assessment of degree of orientation, remote and recent memory for personal and general events, general knowledge, retention of test items, grasp and recall of a test story, and some simple arithmetical tasks. The classification was based also on several weeks of clinical observation so that full allowance was made for failure due to agitation and preoccupation.

Category I: Psychiatric illness not associated with any intellectual impairment or organic brain disease.

Category II: Illness associated with very mild or dubious organic impairment, as indicated, for instance, by slight and doubtful memory defects or personality deterioration.

Category III: Illness associated with organic brain disease, including cases of presenile and senile dementia, of cerebral arteriosclerosis, and chronic G.P.I.

There were no significant differences in mean age for the three groups.

The patients (Table I) showed a striking degree of concreteness, regardless of whether they were considered on clinical grounds to be suffering from an "organic" or a "functional" disorder. Only one patient (who was in Category I) was able to assume the abstract attitude on all three of the Goldstein tests; 54 per cent. were concrete on all three tests, while another 20 per cent. were abstract on two tests and 24 per cent. were abstract on one test. Even on the Colour-Form test, which is usually considered the least difficult, well under half the patients were abstract, though they had all received ample demonstration and modification of the procedure.

Analysis of variance was carried out for the Matrices and Synonyms tests. The Mill Hill Vocabulary scores showed no obvious trend and the difference between the groups was insignificant. The Matrices raw scores were lowest in

TABLE I

Summary of Test Performance in Patient Group
(S.D.s in brackets)

		Clinical Category I	Clinical Category II	Clinical Category III
N		15	18	16
Mean Age		66·93 (5·35)	70·33 (5·95)	69·06 (5·70)
Mean Synonyms Score		18·07 (6·64)	19·72 (6·10)	19·00 (6·93)
Mean Matrices Score		27·60 (8·82)	25·89 (10·69)	22·06 (10·60)
Cube Test	Abstract	5	3	3
	Concrete	10	15	13
Colour-Form Test	Abstract	6	6	5
	Concrete	9	12	11
Colour-Sorting Test	Abstract	2	5	1
	Concrete	13	13	15

the organically impaired group, and highest in the completely unimpaired group, but the differences were not statistically significant. The difference between the Matrices and Vocabulary scores was also taken as a single score comparable with the ratio of verbal to non-verbal score, which is the basis of most current measures of deterioration. The differences between the three groups were again in the expected direction but statistically insignificant. This is not perhaps surprising, as even the "organic" group contained only subjects who could be reliably tested and who were by no means severely demented.

Using only the "abstract-concrete" dichotomy as defined by Goldstein, it was clear that the presence of concreteness in the individual tests was as characteristic of the "functional" disorders of old age as of the psycho-organic illnesses. The fact that so many of the "functional" patients turned out to be concrete in their test performance and thus, according to Goldstein, ought to be looked on as suffering from organic impairment, was the main source of the tests' failure to discriminate between the three clinical groups. Nine out of the eleven cases where the patients had succeeded in adopting the abstract attitude on two or three tests had been placed in Categories I or II by the psychiatrists; the two remaining patients had been allocated to the organic group not on account of any deterioration in mental ability as shown on clinical assessment, but solely on the basis of their histories or neurological findings.

The number of tests in which failure occurred was certainly not related to the severity of the psychiatric disorder. There was, for instance, no tendency for concreteness to be specifically associated with severe depression.

All patients were followed up for at least one to slightly over two years by personal examination (31) or by correspondence with relatives or hospitals (18). Definite evidence of organic cerebral involvement had appeared in only one of the fifteen patients originally classified as without doubt free from brain damage; two cases of the eighteen where there had been some suspicion of early dementia should now be classified as definitely organic, and in all but four of the sixteen organic cases the original classification was confirmed. The outcome of cases can also be classed under three headings: (1) Returned to, and remaining in, usual health; (2) Recurrent ill-health responding to psychiatric in- or out-patient treatment; and (3) Dead, or in chronic hospital or nursing care.

We again find significantly worse outcome in the group of patients originally classified as definitely organic (Table II). Taking clinical groups I and II together, because of the small numbers, $\chi^2=10\cdot3070$, $P=0\cdot01$.

Reclassifying the patients in the light of their later histories did not alter the relationship between clinical judgment and test performance. Thus, the fact that so many of the patients had been markedly concrete in their test performance did not have any prognostic significance, nor did it indicate that they were suffering from any rapidly progressive cerebral disorder.

TABLE II

Outcome in Patient Group

		Clinical Category		
		I and II	III	Total
Outcome	1	15	2	17
	2	12	4	16
	3	6	10	16

(b) *Comparison of A-group with Control Groups B and C:* The composition of the control groups of mentally healthy old people and of normal young adults has already been described, and the test results are summarized in Table III.

TABLE III

Summary of Test Performance in Three Groups

		Age		Synonyms Score		Cube Test			Colour-Form Test		
	N	Mean	S.D.	Mean	S.D.	A_1	A_2	C	A_1	A_2	C
Group A	49	68·88	5·75	18·98	6·23	4	7	38	7	10	32
Group B	49	68·71	6·22	18·51	6·55	9	23	17	9	18	22
Group C	46	26·85	5·77	13·61	7·32	35	5	6	19	13	14

A_1=Abstract at First Attempt.
A_2=Abstract at Final Attempt.
C=Concrete.

They will now be compared with one another and with Group A under separate headings.

(i) *Sex.* There were no significant differences between men and women in any of the three groups.

(ii) *Intelligence.* The only measure applied to all three groups was the Synonyms section of the Mill Hill Vocabulary Test; the difference between the mean scores of the two elderly groups (A: 18·98; B: 18·51) was insignificant, but as was mentioned above, the young adult group was less intelligent (Mean score C: 13·61), this difference being significant at the 0·1 per cent. level (C.R. =3·36).

(iii) *Relationship between Synonyms Score and Ability to Abstract* (*Table IV*). This was assessed by comparing, in each group, the mean Synonyms score of the abstract with the concrete individuals. In all three groups, for the Cube Test, the individuals whose performance was abstract made significantly higher scores than those whose performance was concrete. For the Colour-Form Test, the difference in Synonyms score between abstract and concrete subjects was significant for both of the older groups but not for the young subjects.

TABLE IV

Critical Ratios and Levels of Significance for Differences in Mean Age and Synonyms Score for Abstract and Concrete Subjects

	Age		Synonyms Score	
	Cube Test	Colour-Form	Cube Test	Colour-Form
Group A	Not significant	Not significant	2·32 ($P<0·05$)	2·28 ($P<0·05$)
Group B	2·59 ($P<0·05$)	2·62 ($P<0·05$)	2·74 ($P<0·01$)	2·08 ($P<0·05$)
Group C	Not significant	Not significant	2·06 ($P<0·05$)	Not significant

(iv) *Relationship between Matrices Score and Ability to Abstract.* In the patient group, the only one to whom the Matrices was administered, the abstract subjects made a higher mean score in both the Cube and Colour-Form Tests (raw score differences 8·93 and 5·88 respectively).

(v) *Relationship between Age and Abstractness.* This was assessed by (1) comparing the two groups of young and old normal subjects, and (2) by comparing the mean age of the abstract and concrete individuals in each of the three groups. The older normal group was found to be more concrete than the younger (and less intelligent) one, though the difference was only significant at the 5 per cent. level in both tests (χ^2 for Cube Test 6·0685, for Colour-Form test 5·8797). On both tests, in all three groups, the mean age of the concrete subjects was higher than that of the abstract subjects. The only group in which the differences were significant, however, is that of the older normal subjects (Table IV). It appears that under the age of 40 increasing age may not make serious inroads on the ability to abstract, whereas in the late sixties and early seventies there is a more marked increase in concreteness with age. This trend is less in evidence in our psychiatric patients over 60, who tend to lack the abstract attitude even in the early sixties.

(vi) *Relationship between Psychiatric Illness and Abstractness.* The psychiatric patients were compared with the control group with whom they had been matched for age and sex, and who were of similar intelligence. The Colour-Form test does not discriminate between these two groups ($\chi^2=1·0648$), but on the Cube test the psychiatric patients are more concrete than the normal old people, this difference being significant at the 0·1 per cent. level ($\chi^2=18·2740$).

(vii) *Role of "Learning" and other Factors.* The main feature in which the test procedure described by Goldstein and Scheerer differs from tests used by earlier investigators, is that the subject is given a number of simplified stages, success at which enables him to assume the abstract attitude even if he had been concrete at first presentation of the problem. An attempt was therefore made to find what effect these helping procedures had in producing the various differences found between the three groups. This was done by (1) comparing the groups on their first attempts at the tests, without reference to their performance after the helping stages had been given, and (2) by considering only those patients who were concrete at first, and comparing the groups in respect of their ability to learn the abstract attitude (see Table III).

(1) On the Colour-Form Test, discrimination occurred to the same extent, whether the additional stages were given or not, i.e. the difference between the younger and older normal subjects was significant at the 5 per cent. level in both cases, and between the older normal subjects and patients was not significant in either case. On the Cube Test, discrimination was better between the older and younger subjects if the additional stages were not given (taking into account the first attempt only, $\chi^2=31·7687$), but the additional stages increased

the discrimination between patients and their controls. Classifying according to performance on the first attempt does not discriminate between the two older groups while classifying according to the final performance discriminates at the 0·1 per cent. level. The reason for this would appear to be that there are so few individuals in either group who are abstract at first, that classification according to the first attempt gives only a very limited scope for discrimination.

(2) The subjects who were concrete at the first attempt were divided into two groups: those who after completing the additional stages, were abstract when re-presented with the original instructions, and those who were still concrete. When initially concrete subjects were compared in this way, neither the Cube Test nor the Colour-Form Test discriminated between the younger and older normal subjects. Both tests discriminated at the 1 per cent. level between the psychiatric patients and their elderly controls (χ^2 for Colour-Form Test=8·7330, for Cube Test=16·3050). Both these methods of assessment suggest that the additional stages may be of value, in that they tend to reduce the differences between different age groups and to increase the difference between patients and their controls.

D—Discussion

A number of practical and theoretical points arise from this investigation. From the practical point of view, there is for example the observation that only 28 of the 46 young adults were abstract on both the Goldstein tests given. This is a disturbing observation in view of the following statement in Goldstein and Scheerer's monograph: "Indubitably there is some impairment if the subject fails even in only one of the tests" (p. 30). Although both the occupational level of this group and the fact that the mean Synonym score is lower than that obtained by the two other groups suggest that these controls were somewhat below average intelligence, the findings indicate that it would be rash to diagnose organic impairment in a person of dull or even average intelligence on the basis of failure in the Colour-Form or Cube tests.

Secondly, the diagnostic value of the tests within the patient group is limited to the finding that nine out of the eleven patients who were abstract on two or three out of three tests had been classified by the clinicians as free from definite organic intellectual impairment. Thus the preservation of the abstract attitude in elderly psychiatric patients is evidence against the presence of organic disease or deterioration, but failure to assume the abstract attitude has no diagnostic significance. The tests cannot be used in a positive sense to identify "early dementia".

From the theoretical point of view, there are three findings. First, there is some relationship between intellectual level and the ability to abstract; this is a not unexpected result. Secondly, in the group of mentally healthy old people there was found to be an inverse relationship between age and ability to solve problems in an abstract fashion. Below the age of 68 there was no decline in this ability from the young adult level, but beyond this point there was partial or complete failure on the two Goldstein tests. Only four of the twenty-five subjects over 68 formed exceptions, and none of these was older than 75.

Thirdly, the factor of age does not entirely account for the widespread concreteness among the psychiatric patients. In the case of the Colour-Form test, as there was a negligible difference between patients and controls, the additional factor of psychiatric illness seems to be irrelevant. In the case of the Cube test, the difference between the two groups suggests that psychiatric

illness as well as age is responsible for failures in abstraction; if individuals who were abstract are allocated to the control group and those who were concrete to the patients group, then 70 per cent. of the total number are correctly classified by this test. It is of particular interest that the difference between the groups lay not so much in their capacity to reproduce the designs correctly at first, but in their ability to learn from the simplified presentation.

Organic cerebral disease is not responsible for the difference, as the "organic" patients did no worse than the remainder, with the result that the difference is still significant if the controls are compared only with patient groups I and II. As was shown by the follow-up study, the inability to abstract need not signalize the presence of a rapidly progressing dementing process. The possibility remains that it may indicate a slow general mental decline or senile personality change which has facilitated the occurrence of affective or other psychological disturbance. Against such an assumption is the finding that there was no significant difference in the amount of concreteness between patients who had developed psychiatric illness for the first time late in life, and perhaps in the wake of a hypothetical senile or involutional personality change, and those with a history of attacks of nervous or mental disorders since early adult life.

It has been shown in several recent investigations that changes in cognitive function may be produced by psychiatric illness without either cerebropathological findings or schizophrenic thinking disorder. Hall and Crooks, for instance, (1952) found that neurotic patients, including depressives, did worse than normal controls in verbal and non-verbal learning tests. "They show a marked and significant tendency to lapse in their performance in both tasks, and they tend to forget what they have learned." In our study, in which the majority of patients were suffering from depression, it was again the lack of ability to learn from helping procedures, rather than initial performance, which discriminated the patients from their controls. Inferiority in the performance of a variety of cognitive tests has also been shown to be characteristic both of functional and organic patients when compared with normal people (Shapiro and Nelson, in preparation for publication). It may well be that increased concreteness, in the sense used by Goldstein and his co-workers, is one of several types of cognitive impairment produced by functional psychiatric disorders at all ages.

Summary

Forty-six healthy adults between the ages of 15 and 39, 49 people over 60 without mental disorders or deterioration, and 49 psychiatric patients over 60, were examined for their ability to assume the abstract attitude on some of the tests used by Goldstein and his collaborators. The two groups of subjects over 60 were matched for age and sex.

The following conclusions were reached:

1. A large proportion of young adults were unable to assume the abstract attitude: concreteness appeared to be associated with low verbal ability, but even some subjects of average intelligence as measured by a verbal-test were unable to solve problems in an abstract fashion.

2. In the great majority of mentally healthy subjects, abstract ability was preserved into the second half of the seventh decade; after the age of 68 the abstract attitude became increasingly rare.

3. Psychiatric patients over 60 were significantly more concrete on the Cube test than their controls; most of the patients with a relatively small degree of concreteness were confirmed by follow-up study to be suffering from "functional" psychiatric syndromes, but complete inability to adopt the abstract attitude was not diagnostic of an organic mental disorder.

4. The differentiating value of the Goldstein tests used appears to be limited to the negative finding that preservation of the abstract attitude in elderly people makes the presence of organic cerebral disorder unlikely. Failure in test performance does not necessarily indicate the presence of brain damage.

Finally, it is suggested that research into the relationship of abstract behaviour with age, general mental ability, learning ability, and the presence of psychological disorders, might be profitable.

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THE RELIABILITY OF PSYCHIATRIC, AND THE VALIDITY OF PSYCHOLOGICAL, DIAGNOSES

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The Problem

Criterion of Value

In determining the diagnostic value of psychological tests the usual external criterion is the psychiatric diagnosis. This criterion has suffered a steady decline in prestige among both psychiatrists and psychologists. The following remarks by Noyes (1953) would be endorsed by many psychiatrists: "The principal value of classification is not in the categorizing of a disease entity but in quickly eliminating those considerations which will be least useful in understanding the patient and in directing attention to those which are likely to be relevant. Except in organic disorders a classificatory diagnosis is less important than a psychodynamic study of the personality. The psychiatrist should be interested in processes, not in labels . . . we should endeavour not so much to fit the symptoms into a classificatory scheme as to understand the sick person in terms of his life experience."

This is primarily the point of view of the clinician of psychoanalytic or psychobiological leanings and plenty of time to spare and illustrates the vast gap that too often exists between clinician and research worker.

When the psychiatrist has made psychodynamic studies of several personalities, he must, if he is to formulate a cohesive, teachable body of knowledge, compare one with another. With comparison comes classification; without it comes a tendency to feel things in one's bones and such rheumatoid sensitivity is notoriously difficult to convey to the tyro.

Psychologists too attack the present psychiatric nosology.

Roe (1949) writes: "I suggest that much of this research (the use of various psychological devices for making psychiatric diagnoses) is not only a waste of time, and a perpetuation of errors, but is actually preventing advance in the field. There are many reasons why this is true, but one of the most potent is that it involves clinging to a classification which has long since been outlived. I submit that using techniques which are not too precisely validated at all, to place patients in psychiatric categories, the inadequacy of which is admitted by all concerned, is a treadmill procedure guaranteed to keep us moving in circles."

Many psychiatrists, as well as psychologists, would agree with this estimate of psychiatric nosology and psychological practice and yet the curious fact is that there seems to be little or no evidence for this belief. Whether or not such diagnoses are useful, no other classificatory system has been advanced and supported by experimental evidence.

Roe states that the most potent reason for not using tests for diagnostic purposes is that psychiatric classification has long since been outlived. Apart from the fact that classification was never viable and could not, therefore, be outlived, the statement, even with the substitution of the word outmoded, is palpably false. Such classification is still in fact very widely used. The additional statement that the inadequacy of psychiatric categories is admitted

by all concerned is a rather subtle misuse of words. Inadequacy is no reason for abandoning, unless something more adequate can be substituted. One still has the possibility of making the inadequate more adequate. An adequate reason for abandoning existing categories would be their unsuitability. If our supply of Burgundy were inadequate, we would strive to make it more adequate by ordering more and better vintages; if our supply were unsuitable—for example, all the bottles were corked—we would abandon it and strive to obtain something more suitable.

The position then is that the inadequacy of psychiatric nosology is probably recognized by all concerned, but its unsuitability is not so recognized. Many citations could be made to justify this view, but two will suffice. Zubin (1953) writes: "While the reaction-pattern type of model to explain the etiology of neurosis is an attractive one, it does not lend itself as readily to experimental manipulation as the disease-entity model with the potential physiological, biochemical and genetic factors that enter into the postulation of disease models. If one regards the problem, not as a search for basic etiology, but as a search for serviceable models leading to further knowledge about etiology . . . the disease model is to be preferred." Again, Wittenborn (1951) writes: "If a well-formulated logically coherent theory for the psychoses were available, the intervening variables of this theory could provide the basis for economical description. Since no such theory is available, any phenomenal clustering tendency provides a plausible conceptualization and allows us to use some of the advantages of theory, i.e. measurement based on intervening variables . . . The manifestation of symptom clusters, regardless of the exact conditions responsible for their appearance, takes us a step nearer to our goal."

Is this psychodiagnostic procedure guaranteed to keep us moving in circles? It may do so; but it is certainly not guaranteed to do so. If it should turn out that the test categories agree in the main with reasonably reliable psychiatric categories, then the way is opened up for the description and measurement by means of these tests of the attributes of these categories. This is not an unimportant task for the psychologist. As a matter of fact Wittenborn has shown in a number of factorial studies, using a specially designed rating scale, that the factors he has been able to extract are rather congruent with the well-known psychiatric categories (Wittenborn, 1951) and that this holds even when employing psychiatrists from different institutions (Wittenborn, 1952). A study of these factors may well help us to isolate underlying processes which can be brought under experimental control. There seems then no reason for agreeing with Noyes that psychiatrists should be more interested at this stage in processes than in labels.

If psychiatric diagnoses are to be used as a criterion, obviously they must be reliable. Although psychiatric diagnosis is crucial to perhaps the majority of psychiatric, and to many psychological, researches, this vital question of reliability has scarcely been studied at all.

Ash (1949) reports agreement on major diagnostic categories between pairs of psychiatrists of 58 per cent. to 67 per cent. and on specific categories of 31½ per cent. to 43½ per cent. This is regarded as discouraging. There are, however, a number of unusual features in this study which make the results an unreliable guide for most psychiatric practice. Only 35 of the 139 cases were said to have indicated a clear-cut psychopathology, interviewing was carried out jointly and categories were used which were not mutually exclusive. Among specific categories—for example Psychopaths—are found schizoid, constitutional inferiority, drug addiction, epileptoid, etc. Clearly there is no reason why

a schizoid psychopath should not exhibit constitutional inferiority and be a drug addict. When account is taken of these facts, it is not surprising that the figures are low.

The studies by Doering (1934) and by Mehlman (1952) both utilize diagnoses made in the ordinary course of clinical work. Whilst no doubt such diagnoses should always be made with as much care as possible, it cannot be concluded from such studies that psychiatrists are incapable of making reliable assessments when put on their mettle. In addition, no preliminary discussion to clear up any semantic difficulties was possible in these studies. Masserman and Carmichael (1938) found that a major revision of diagnosis was necessary in 40 per cent. of cases within a year. These again were ordinary workaday diagnoses.

Hunt, Wittson and Hunt (1953) report on a series of Service Personnel. They estimated the agreement between psychiatrists at the Pre-Commission Station and at the Hospital to which the cases were subsequently sent. The diagnoses were virtually uncontaminated. Agreement on unsuitability for further service—a relatively easy task—was 94 per cent., about which there could be no complaint. The average agreement on the major categories: Psychosis, Psychoneurosis, Personality Disorder, was 54 per cent. and on specific categories 33 per cent. This again is treated as discouraging; but once more categories were used which were not mutually exclusive. Among Psychoneurotics are to be found the following: mixed, anxiety, unclassified, hysteria, situational, neurasthenia, psychasthenia, traumatic, hypochondria, inadequate, reactive depression. Logically this is like asking "Is this an elephant? (If so, what sort?) *or* is it from Africa? *or* from not very good stock? *or* a bit of each? *or*, if you don't know, say so". In other words, there are at least three distinct principles of division, one denial of these principles and one expression of inability to apply these principles.

The authors went on to examine the changes in diagnosis between the two centres and these were found to be rather consistent. As they put it, "the changes were nearly all neighbourly changes which did not involve much clinical displacement and raise the question as to whether the 'practical' reliability of the diagnosis (in terms of the care, treatment and disposition of the cases) is not larger than our 'pure' statistics would indicate." This raises another question, which does not appear to have been dealt with at all, whether the use in all these studies of a simple dichotomy of agreement—disagreement is inadequate, if not unsuitable. If one psychiatrist makes a diagnosis of Paranoid Schizophrenia, another of Paraphrenia and a third of Hysteria, there would almost certainly be general agreement that the views of the first two psychiatrists were much closer together than that of either with the third. A Scale, which takes account of partial agreement, is, therefore, necessary. In the present state of our knowledge such a scale inevitably lacks experimental support. This may be remedied as more studies of the type conducted by Eysenck (1952) and Wittenborn (1951) become available.

The Value of Psychological Tests

How far do the results of psychological tests, when administered first by the same psychologist and then by different psychologists, agree with the initial and final psychiatric diagnoses? In other words, do psychologists gain by observing the patient during the testing session? Do psychologists in fact gain by testing patients at all or could they diagnose just as well on the basis of knowledge of the type of patients admitted to a particular division and of the

age of each particular patient? Can psychologists be of any diagnostic assistance to psychiatrists?

The Procedure

In order to elicit information relevant to the above problems, it was necessary for at least two psychiatrists to diagnose the subjects independently, for tests to be administered and interpreted first by the same psychologist (without any information other than the subject's age), then by different psychologists (without any information other than age and sex), for a final diagnosis to be agreed upon by the two psychiatrists and for a scale ranging from complete agreement to complete disagreement to be employed.

Psychiatric Diagnosis

Approximately one week after admission each patient was interviewed independently by each psychiatrist. Otherwise the usual diagnostic procedure was employed. Both had available, for example, the Psychiatric Social Worker's report and any other relevant information which might have been supplied. No discussion of the patient took place until each psychiatrist had recorded his diagnosis and deposited it with the Ward Sister or Charge Nurse. Just before the patient's discharge or after approximately one to two months, the two psychiatrists discussed the case together and arrived at a final diagnosis. They remained in ignorance of the test results.

Had the main purpose of the investigation been the assessment of the reliability of psychiatric diagnoses, the final diagnosis would, of course, have been made independently by each psychiatrist. For the present purpose of ascertaining the validity of the tests it was considered that any disadvantages accruing from contamination would be offset by the probable strengthening of the final criterion.

Since it is scarcely feasible to obtain a chance score with which to compare the psychiatric and psychological diagnoses, it was decided to ask a psychiatrist and a psychologist to "guess" the diagnoses. Both of them were familiar with the type of patients admitted to each of the two Divisions and both were provided with the age and sex of the patient. Obviously such information should enable one to make better than chance guesses.

There were seven participants altogether—the Consultant Psychiatrist and the Senior Hospital Medical Officer on each Ward, the Psychiatric Research Fellow, who did the guessing, and two Psychologists. The Consultant Psychiatrists are henceforward referred to as A, the SHMOs as B, the Experimenter as E, the psychiatric "guesser" as X and the psychological "guesser" as Y. E was, in fact, a dual personality, since he was also Y. The agreement between them was, however, not impressive and it may safely be concluded that the dissociation was rather complete.

Psychological Testing

Testing was carried out on the average four days after admission. The tests, in their usual order of administration, were: The Porteus Mazes (with the method of administration and scoring described by Foulds (1951)); the Mill Hill Vocabulary Scale, four pictures from the Thematic Apperception Test (with the method of administration and scoring described by Foulds (1952)) and the Progressive Matrices. The ratio between the Matrices and Mill Hill tests has been found to be of some diagnostic value (Foulds, 1953; Himmelweit, 1945).

During the sessions in which the investigator also administered the tests, subjects were discouraged from entering into any discussion not immediately relevant to the tests. This discouragement was almost completely successful.

The Diagnostic Agreement Scale

The following diagnostic categories were used in this study:

- Paranoid State
- Schizophrenia
  - Paranoid
  - Katatonic
    - Excitement
    - Stupor
  - Hebephrenic
  - Simple
- Manic-Depressive
  - Manic
  - Melancholia
- Organic
- Schizoid Psychopath
- Dysthymia
  - Obsessional
  - Reactive Depression
  - Anxiety State
- Hysteria

The following diagnostic pairs were treated as identical:

Mania—Hypomania
Paranoid State—Paraphrenia
Hysteroid Psychopath—Hysteria
Manic-Depressive, Depressive State—Melancholia
Anxiety Hysteria—Hysteria with Anxiety features

The following diagnostic pairs were treated as similar:

Paranoid State—Paranoid Schizophrenia
Involutional Paranoid State—Involution Melancholia
Paranoid Schizophrenia—Katatonic Schizophrenia
Paranoid Schizophrenia—Hebephrenic Schizophrenia
Paranoid Schizophrenia—Simple Schizophrenia
Katatonic Schizophrenia—Hebephrenic Schizophrenia
Katatonic Schizophrenia—Simple Schizophrenia
Hebephrenic Schizophrenia—Simple Schizophrenia
Simple Schizophrenia—Schizoid Psychopath
Melancholia—Reactive Depression
Reactive Depression—Obsessional
Reactive Depression—Anxiety State
Obsessional—Anxiety State

The remaining 65 possible pairs were treated as different.

The method of scoring the scale was as follows:

Diagnoses Identical ..	4	Features Identical ..	2
Diagnoses Similar ..	2	Features Similar ..	1
Diagnoses Different ..	0	Features Different ..	0

If Diagnosis and Features have been reversed, both possible reversals are scored and two added if the unreversed Diagnoses are similar. Thus: Diagnosis Similar, but Diagnosis and Features reversed, otherwise Identical and Different

(or Different and Identical). E.g. Anxiety State with hysterical Features and Reactive Depressive with Anxiety Features would be scored: 2, 4, 2. The mean is then taken (to the nearest whole number) i.e. 3. Again, Diagnosis Different, Diagnosis and Features reversed, otherwise Identical and Similar—e.g. Anxiety State with Hysterical Features and Hysteria with Depressive Features would be scored: 0, 5, 4, the final score being the mean of 3.

Each of the possible score categories is illustrated below, thus:

1. *Diagnosis and Features identical* — *Score* 6
   - A. Anxiety State with Depressive features
   - B. Anxiety State with Depressive features
2. *Diagnosis identical and no Features mentioned* — *Score* 6
   - A. Conversion Hysteria
   - B. Conversion Hysteria
3. *Diagnosis identical and Features similar* — *Score* 5
   - A. Obsessional with Anxiety features
   - B. Obsessional with Depressive features
4. *Diagnosis identical and Features different* — *Score* 4
   - A. Reactive Depressive with Obsessional features
   - B. Reactive Depressive with Hysterical features
5. *Diagnosis identical and Features mentioned in one only* — *Score* 4
   - A. Reactive Depressive with Obsessional features
   - B. Reactive Depressive
6. *Diagnosis similar with Features identical* — *Score* 4
   - A. Paranoid Schizophrenia with Obsessional features
   - B. Paraphrenia with Obsessional features
7. *Diagnosis similar with Features not mentioned* — *Score* 4
   - A. Paranoid Schizophrenia
   - B. Paraphrenia
8. *Diagnosis similar and Diagnosis and Features reversed, otherwise identical* — *Score* 5
   - A. Anxiety State with Depressive features
   - B. Reactive Depressive with Anxiety features
9. *Diagnosis similar and Features similar* — *Score* 3
   - A. Schizoid Personality with Anxiety features
   - B. Simple Schizophrenia with Depressive features
10. *Diagnosis and Features reversed, otherwise identical* — *Score* 4
    - A. Anxiety State with Obsessional features
    - B. Obsessional with Anxiety features
11. *Diagnosis similar and Diagnosis and Features reversed, otherwise identical and different* — *Score* 3
    - A. Anxiety State with Obsessional features
    - B. Reactive Depressive with Anxiety features
12. *Diagnosis similar and Diagnosis and Features reversed, otherwise identical and Features mentioned in one only* — *Score* 3
    - A. Anxiety State
    - B. Reactive Depressive with Anxiety features
13. *Diagnosis similar and Features different* — *Score* 2
    - A. Melancholia with Paranoid features
    - B. Reactive Depressive with Obsessional features
14. *Diagnosis similar and Features mentioned in one only* — *Score* 2
    - A. Melancholia with Paranoid features
    - B. Reactive Depressive
15. *Diagnosis different, but Features identical* — *Score* 2
    - A. Anxiety State with Obsessional features
    - B. Schizophrenia with Obsessional features
16. *Diagnosis and Features reversed, otherwise identical and similar* — *Score* 3
    - A. Anxiety State with Hysterical features
    - B. Hysteria with Depressive features
17. *Diagnosis and Features reversed, otherwise similar* — *Score* 2
    - A. Melancholia with Paraphrenic features
    - B. Paranoid Schizophrenia with Depressive features

18. *Diagnosis different, but Features similar* — *Score* 2
    A. Obsessional with Anxiety features
    B. Hysteria with Depressive features
19. *Diagnosis and Features reversed, otherwise identical and different* — *Score* 2
    A. Anxiety State with Obsessional features
    B. Hysteria with Anxiety features
20. *Diagnosis and Features reversed, otherwise identical and Features mentioned in one only* — *Score* 2
    A. Anxiety State
    B. Hysteria with Anxiety features
21. *Diagnosis and Features reversed, otherwise similar and different* — *Score* 1
    A. Melancholia with Paranoid features
    B. Obsessional with Depressive features
22. *Diagnosis and Features reversed, otherwise similar and Features mentioned in one only* — *Score* 1
    A. Melancholia
    B. Obsessional with Depressive features
23. *Diagnosis and Features different* — *Score* 0
    A. Schizophrenia with Obsessional features
    B. Melancholia with Paranoid features
24. *Diagnosis different and Features mentioned in one only* — *Score* 0
    A. Schizophrenia with Obsessional features
    B. Melancholia
25. *Diagnosis different and no Features mentioned* — *Score* 0
    A. Melancholia
    B. Hysteria

The Scale is clearly lacking in experimental support for the attribution of similarity to the various diagnostic pairs and for the particular weightings given to the scores. Improvements will have to wait upon further research. In the meantime the Scale does appear to give a more accurate measurement of agreement than any simple dichotomy of agreement–disagreement is likely to do.

The Subjects

The subjects were successive admissions to two of the Divisions of the Hospital, one containing both male and female Wards, the other male only.

The only cases deliberately excluded were those who had been tested at one or other of the Out-patient Departments prior to admission and those suffering from a disparate physical illness. In fact five other cases were missed because the psychiatrist decided that immediate treatment was necessary. Since these five were classical cases, their exclusion has almost certainly reduced the agreement both between psychiatrists and between psychiatrists and psychologist. One further case was omitted because he could not be induced to do any of the tests at all. Those who did something, but not everything on the tests were included. Finally one case was omitted because the Charge Nurse inadvertently asked the psychologist to test the patient on the Ward as he was an Epileptic.

Results

Eighteen Cases in Which the Tests were Administered and Interpreted by the Same Psychologist

Table I shows the amount of agreement for each of the ten pairings.

Table I

Agreement Between Diagnosticians in 18 Cases Tested and Diagnosed by the Same Psychologist

	A:B	A:E	B:E	A:X	A:Y	B:X	B:Y	E:X	E:Y	X:Y
Mean	3·78	4·06	4·11	2·17	2·56	2·33	2·33	1·61	2·06	2·61
S.D.	1·84	1·81	1·45	1·98	1·77	2·11	2·08	1·64	2·20	2·19

A—Consultant Psychiatrist; B—SHMOs; E—Experimenter; X—Psychiatric "guesser"; Y—Psychological "guesser".

Table II shows the t (for correlated means) and P values for comparisons derived from Table I.

TABLE II

t and P Values for Comparisons Derived from Table I

	t	P		t	P		t	P
AB and AE	=0·62	>·1	AE and BE	=0·12	>·1	BE and AX	=3·23	<·01
and BE	=0·82	>·1	and AX	=2·59	<·02	and AY	=2·98	<·01
and AX	=2·30	<·05	and AY	=2·14	<·05	and BX	=2·78	<·02
and AY	=2·30	<·05	and BX	=2·93	<·01	and BY	=3·18	<·01
and BX	=2·42	<·05	and BY	=2·98	<·01	and EX	=5·21	<·001
and BY	=3·02	<·01	and EX	=4·30	<·001	and EY	=3·60	<·01
and EX	=3·81	<·01	and EY	=3·03	<·01	and XY	=2·94	<·01
and EY	=2·97	<·01	and XY	=2·74	<·02			
*and XY	=1·92	<·1						

There were thus 21 comparisons between two psychiatrists (or a psychiatrist and the experimenter) on the one hand and a psychiatrist (or the experimenter) and a "guesser" on the other hand. Of these 21 comparisons one (AB and XY) failed to reveal a difference significant at the 5 per cent. level of confidence; 4 were significant at the 5 per cent. level of confidence; 3 were significant at the 2 per cent. level; 11 at the 1 per cent. level and 2 at the 0·1 per cent level.

There were 3 comparisons between the psychiatrists and the experimenter and none of these was significant even at the 10 per cent. level of confidence.

The two psychiatrists who investigated the patients and the experimenter were, therefore, more or less equally successful in reaching agreement among themselves at a level well above that achieved by the "guessers".

Table III shows the amount of agreement between the experimenter and the final psychiatric diagnosis and between each of the "guessers" and the final psychiatric diagnosis.

Table IV shows the t and P values for comparisons derived from Table III.

TABLE III

Agreement Between the Final Psychiatric Diagnosis and the Experimenter and the Two "Guessers"

	E:C	X:C	Y:C	
Mean	4·50	1·94	2·22	C—Criterion diagnosis
S.D.	1·72	1·87	1·96	

TABLE IV

t and P Values for Comparisons Derived from Table III

		t	P
EC and XC	=	4·06	<·001
EC and YC	=	3·45	<·01
XC and YC	=	0·58	>·1

The agreement between the experimenter and the final psychiatric diagnosis differed at the 0·1 per cent. level of confidence from "guesser" X and the final psychiatric diagnosis and at the 1 per cent. level from Y and the final diagnosis.

Eighteen Cases in Which the Tests were Administered and Interpreted by Different Psychologists

Table V shows the amount of agreement for each of the ten pairings (as in Table I).

Table VI shows the t and P values for comparisons derived from Table V.

TABLE V

Agreement Between Diagnosticians in 18 Cases Tested and Diagnosed by Different Psychologists

	A:B	A:E	B:E	A:X	A:Y	B:X	B:Y	E:X	E:Y	X:Y
Mean	4·44	3·67	3·44	1·67	2·00	1·33	1·61	2·11	2·11	2·11
S.D.	1·71	1·79	2·03	1·92	1·86	1·79	1·92	1·94	1·83	1·41

TABLE VI

t and P Values for Comparisons Derived from Table V

	t	P		t	P		t	P
AB and AE	=1·60	>·1	AE and BE	=0·83	>·1	BE and AX	=2·64	<·02
and BE	=2·02	<·1	and AX	=3·08	<·01	and AY	=2·25	<·05
and AX	=3·79	<·01	and AY	=2·32	<·05	and BX	=3·40	<·01
and AY	=3·30	<·01	and BX	=3·97	<·001	and BY	=3·27	<·01
and BX	=4·78	<·001	and BY	=3·55	<·01	*and EX	=1·66	>·1
and BY	=4·35	<·001	and EX	=2·29	<·05	*and EY	=1·96	<·1
and EX	=3·15	<·01	and EY	=2·69	<·02	and XY	=2·25	<·05
and EY	=3·70	<·01	and XY	=2·94	<·01			
and XY	=4·02	<·001						

Of the 21 comparisons between two psychiatrists (or a psychiatrist and the experimenter) on the one hand and a psychiatrist (or the experimenter) and a "guesser" on the other hand, 2 failed to reveal a difference significant at the 5 per cent. level of confidence; 4 were significant at the 5 per cent. level; 2 at the 2 per cent. level; 9 at the 1 per cent. level and 4 at the 0·1 per cent. level.

Of the 3 comparisons between the psychiatrists and the experimenter none was significant at the 5 per cent. level of confidence.

The two psychiatrists, who investigated the patients, and the experimenter, who interpreted the tests without seeing the patients, were successful in reaching agreement among themselves at a level well above that achieved by the "guessers".

Table VII shows the amount of agreement between the experimenter and the final psychiatric diagnosis and between each of the "guessers" and the final psychiatric diagnosis.

Table VIII shows that the t and P values for comparisons derived from Table VII.

TABLE VII

Agreement Between the Final Psychiatric Diagnosis and the Experimenter and the Two "Guessers"

	E:C	X:C	Y:C
Mean	3·83	1·28	2·00
S.D.	1·83	1·63	2·24

TABLE VIII

t and P Values for Comparisons Derived from Table VII

	t	P
EC and XC	4·40	<·001
EC and XC	2·69	<·02
XC and YC ..	1·11	>·1

The agreement between the experimenter and the final psychiatric diagnosis differed at the 0·1 per cent. level of confidence from "guesser" X and the final psychiatric diagnosis, and at the 1 per cent. level from "guesser" Y and the final psychiatric diagnosis.

The experimenter may, therefore, be seen to have been somewhat less successful in his diagnostic predictions when he did not see the patients. The difference was not, however, statistically significant.

Discussion

The unreliability of psychiatric diagnoses has been assumed without adequate experimental support. In the present investigation there was a minority of cases in which agreement by any standard would have to be regarded as poor. These are probably the cases which are discussed most frequently and which are presented at Case Conferences, thus contributing to a biassed impression. The problem is not so much can psychiatrists reach agreement on diagnoses, but under what circumstances can they reach agreement and with what sort of people?

Some such scale of diagnostic agreement as the one used in this study seems to be essential. It is suggested that only those cases which have a sufficiently high mean rating score when diagnosed independently by three psychiatrists should be used in any research investigation in which the diagnosis is crucial. This is a stringent requirement; but it would have at least two important advantages: firstly, it would discourage premature publication of findings which could not be other than inconclusive and secondly, it would, by increasing the homogeneity of groups almost certainly reduce the variability of measures, thus enabling the investigator to differentiate more precisely between smaller groups. The rejected cases could, of course, be included as a separate group and their scores might be expected to fall somewhere between the extremes of any two groups which had been clearly differentiated.

In the setting of the present investigation the extent of agreement between psychiatrists, three out of four of whom had been working together for some years, did not appear to be too discouraging and could almost certainly be increased by more thorough discussion of semantic difficulties. Agreement between either psychiatrist and a psychologist using a short battery of tests (taking on the average about one and a half hours in all) was of about the same order. It would appear, therefore, that the psychologist, even when he does not make use of a Social History, etc., may be engaging in a reasonably meaningful and possibly even useful activity.

Summary and Conclusions

Criticisms of psychiatric nosology have been discussed and it has been argued that, whilst its inadequacy is generally admitted, its unsuitability has not been demonstrated.

Agreement between psychiatrists making independent diagnoses was in the region of 4 on a scale ranging from 0 to 6. Illustrations of the type of agreement represented by a score of 4 can be seen in the Appendix.

Using the agreed final psychiatric diagnosis as criterion, diagnostic predictions were made from a short battery of tests. When the psychologist interpreted and administered the tests, agreement was 4·50 on the Scale. When he made the diagnoses from the tests without seeing the patient, agreement was 3·83. The difference between the two series was not significant. Diagnoses based on knowledge of the type of patients admitted and of the age and sex of the particular patients showed a mean agreement with the criterion diagnosis of less than 2 on the scale.

In the setting of this investigation it would appear that the reliability of psychiatric, and the validity of psychological, diagnoses are not as poor as current opinion would lead one to suppose. The reader can form his own judgment from the list in the Appendix of diagnoses made on the 18 cases which were seen by two psychiatrists and the experimenter.

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APPENDIX

Cases diagnosed by a Consultant Psychiatrist (A), a Senior Hospital Medical Officer (B) and the Experimenter (E)

		Major Diagnosis	Features	Scores
1.	(A)	Anxiety-Hysteria	Depressive	AB.3
	(B)	Reactive Depression	Hysterical and Obsessional	AE.3
	(E)	Obsessional	Hysterical	BE.4
2.	(A)	Anxiety-Hysteria		AB.6
	(B)	Anxiety-Hysteria		AE.3
	(E)	Reactive Depression	Hysterical	BE.3
3.	(A)	Reactive Depression	Anxiety	AB.5
	(B)	Anxiety State	Depressive	AE.5
	(E)	Anxiety State	Depressive	BE.6
4.	(A)	Melancholia	Paranoid	AB.1
	(B)	Hysteria	Depressive	AE.5
	(E)	Paraphrenia	Melancholic	BE.2
5.	(A)	Reactive Depression	Hysterico-Psychopathic	AB.4
	(B)	Hysteria	Depressive	AE.6
	(E)	Reactive Depression	Hysterical	BE.4
6.	(A)	Reactive Depression	Hysterical	AB.2
	(B)	Paraphrenia	Depressive and Hysterical	AE.2
	(E)	Paraphrenia	Hysterical	BE.5
7.	(A)	Schizoid Personality	Obsessive	AB.4
	(B)	Schizophrenia	Obsessive and Anxiety	AE.6
	(E)	Schizoid Personality	Obsessive	BE.4
8.	(A)	Schizophrenia Simplex		AB.4
	(B)	Schizoid Psychopath		AE.6
	(E)	Schizophrenia Simplex		BE.4
9.	(A)	Melancholia		AB.0
	(B)	Hysteria		AE.2
	(E)	Reactive Depression	Hysterical	BE.2
10.	(A)	Reactive Depression	Anxiety	AB.4
	(B)	Reactive Depression	(Alcoholism)	AE.3
	(E)	Anxiety State		BE.4
11.	(A)	Anxiety-Hysteria		AB.6
	(B)	Anxiety-Hysteria		AE.5
	(E)	Hysteria	Obsessive	BE.5
12.	(A)	Melancholia	Psychopathic	AB.2
	(B)	Reactive Depression		AE.2
	(E)	Reactive Depression	Anxiety	BE.4
13.	(A)	Manic-manic-depressive	Depressive	AB.4
	(B)	Manic-manic-depressive		AE.4
	(E)	Manic-manic-depressive		BE.6
14.	(A)	Manic-manic-depressive		AB.6
	(B)	Manic-manic-depressive		AE.6
	(E)	Manic-manic-depressive		BE.6
15.	(A)	Paranoid Schizophrenia	(Homosexual)	AB.4
	(B)	Paranoid Schizophrenia	Depressive	AE.6
	(E)	Paranoid Schizophrenia	(Homosexual)	BE.4

		Major Diagnosis	Features	Scores
16.	(A)	Hebephrenic Schizophrenia		AB.6
	(B)	Hebephrenic Schizophrenia		AE.6
	(E)	Hebephrenic Schizophrenia		BE.6
17.	(A)	Hebephrenic Schizophrenia		AB.4
	(B)	Hebephrenic Schizophrenia	Paranoid	AE.0
	(E)	Psychopath	Paranoid	BE.2
18.	(A)	Schizophrenia Simplex	Depressive	AB.3
	(B)	Paranoid Schizophrenia	Simplex	AE.3
	(E)	Paranoid Schizophrenia	Anxiety	BE.4

INTELLECTUAL AND RORSCHACH TEST PERFORMANCES OF A GROUP OF SENILE DEMENTIA PATIENTS AND OF A GROUP OF ELDERLY DEPRESSIVES

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Introduction

Owing to the increase in the expectancy of life, there is an increase in the incidence of aged people suffering from mental illness who are admitted to hospital. This has stimulated the paying of special attention to the problems of differential diagnosis in order to avoid lengthy hospitalization wherever possible. Recent studies have tended to emphasize the frequency of affective disorders as well as senile dementia in aged patients. It is consequently important to distinguish the former group because of the greater possibilities of treatment there than in senile dementia. A recent paper (O'Connell, 1954) has been concerned with the study of case material of patients over the age of sixty admitted to this hospital. The present study is largely based on material obtained from patients drawn from O'Connell's sample, but also includes cases with longer hospitalization.

Psychological Studies of the Aged

Psychological studies with old people have been mainly concerned with the related questions of intellectual decline with age and of pathological intellectual deterioration.

Details are available in the work of several authors (see Miles and Miles, 1932; Wechsler, 1944; Foulds, 1949) of the normal variations of intellectual and verbal ability with age. Broadly speaking, it has been shown that intellectual ability increases during childhood up to the age of fourteen, remains constant for about ten years and then progressively declines with age as far as normative material is available. Verbal ability on the other hand, increases steadily until middle age and even in later years only shows a small decline. Normative material, however, is only available up to the age of 60 to 65.

An abnormal discrepancy between any person's performances on intellectual and verbal tests (after allowing for normal age variations) has formed the basis for an estimation of intellectual deterioration (see Babcock, 1930; Shipley, 1941; Wechsler, 1944), the thesis being that organic impairment, and to a lesser degree functional disorders, result in an impairment of intellectual ability whereas verbal ability remains relatively free from impairment. Another development has been the attempt to equate types of wrong answers to intellectual tests with the degree of clinical deterioration (Pinkerton and Kelly, 1952; Bromley, 1953).

Difficulties are immediately encountered with old people in estimating intellectual level and deterioration because of the lack of normative data for the advanced age ranges. These data are necessary in differentiating normal and abnormal changes of intellectual and verbal abilities in advancing age, it being

assumed that senile dementia should present intellectual deterioration as a distinguishing feature.

Important here is the further assumption that the relative stability of verbal ability (and its consequent use, from the investigations of Foulds (1949) and Raven (1947, 1948), in estimating what appears to be a person's pre-deterioration level of ability) still holds in senile dementia, which is thus identified with advanced age, although this latter assumption has not been demonstrated.

Several studies have illustrated that verbal ability is impaired in age, but this impairment is difficult to measure owing to the wide range of acceptable definitions for any particular word (see Brody, 1942; Yacorzynski, 1941; Cleveland and Dysinger, 1944; Acklesberg, 1944).

Finally, there is the question of test reliability. With any mental illness, intellectual test-retest reliability appears to be reduced (see Desai (1952) for example). A similar reduction may also occur when there is a low level of ability, as indicated in the performance of normal children (Raven, 1947, 1948), and in senility (Eysenck, 1945). M. D. Eysenck observed that this reduced reliability is partly caused by the correct solution of problems on one occasion but not on a previous or subsequent occasion. I had observed this feature myself in the course of ordinary clinical work. In these cases, it seemed that the decreased test-retest reliability is at least partly explained by what appears to be a function fluctuation of performance with intellectual tests.

A number of systematized personality studies with old people, using the Rorschach test as the method of investigation, have been reported (W. G. Klopfer, 1946; Prados and Fried, 1947; Chesrow *et al.*, 1949; Dorken and Kral, 1951; Ames *et al.*, 1954). Table IV gives a brief summary of the findings. These different studies all show that in old age there is a reduction in responsiveness, a marked limitation of both creativity and affective response, with little awareness of conflict. With senile dementia, these limitations become even more marked, although there is again a difficulty in distinguishing between normal and abnormal personality in old age. It will be seen from the previous discussion that a comparison of Rorschach test performances of elderly depressives with senile dementia would be useful.

The present investigation was therefore designed to elicit the performance of senile dementias and elderly depressives with regard to the above problems concerning intellectual and personality characteristics in advanced age.

Method

Suitable patients over the age of 60 were interviewed and tested. From these a group of 25 senile dementias and a group of 24 elderly depressives were extracted. No patients were included in either of these groups when the case was thought to present complicating features. This entailed the exclusion, for example, of cerebral arteriosclerotic and schizophrenic cases.

Each patient initially performed the Progressive Matrices (1947), Sets A, Ab, B, Book Form, and the Mill Hill Vocabulary Scale (Oral Definitions Form), as measures of intellectual and verbal ability. The Rorschach test was also administered. After a short interval of five or six days the Progressive Matrices was re-administered. Patients who were completely incapable of performing any test, and also those whose performances showed no more than a passive selection of answers, were subsequently excluded from the groups finally studied. The implications of this selection will be discussed later.

Previous estimations of the function fluctuation of abilities as reflected by a low test-retest reliability have only made use of the total scores obtained (e.g. Thouless, 1936). This tends to obscure fluctuations of ability within a test performance as it does not make allowance for the type of fluctuation previously noted here. A more suitable method was accordingly undertaken. With this method each patient's performance on the Progressive Matrices was plotted along the order of difficulty of the test's problems obtained in its standardization with normal children. By this method it is possible to assess each patient's maximum potential of intellectual ability disregarding losses during performance caused by an apparent fluctuation of ability. With little or no fluctuation present, this maximum potential of ability should approximately equal the actual test score, but with increasing fluctuation there will be an increasing discrepancy between the two different measures.

A standard procedure was adopted in fixing the point of maximum potential in order to reduce the possibility of including the selection of correct answers by chance. This consisted of taking the last point where a particular problem was correctly solved on both testing occasions, or alternatively, where the last pair of consecutive problems was correctly solved on either testing occasion. Isolated problems correctly solved past this point were included if there were not more than two consecutive intervening failures. They were also included if there was not more than one intervening failure from the last already accepted problem.

The method of administering and scoring the Rorschach test was that described by Klopfer and Kelley (1942).

Data were now available for each patient concerning five variables—age; Progressive Matrices, first and second testing; Progressive Matrices, maximum potential score; Mill Hill Vocabulary Scale; and for the Rorschach Test.

Results (Intellectual Tests)

From Table I, it can be seen that in age, intellectual and verbal performance, the two groups are drawn from different populations in all respects. The senile dementia group is distinctly older and does less well on both intellectual and verbal tests. With both groups there is a fluctuation of intellectual ability present. This is most marked in the senile dementia group. Their maximum potential Progressive Matrices score is not only higher than their actual performance; it is also much more comparable to the depressives' score. It is therefore reasonable to assume that relative to the depressive, the senile patient fluctuated more in productivity whatever his potentiality for observation and clear thinking happened to be.

Table I

Mean Scores of Variables

	Age	P.M.$_1$	P.M.$_2$	P.M. Maximum	M.H.V.S.
Senile	73·84	15·00	15·36	25·32	41·64
Depressive	68·17	22·92	23·67	29·75	53·08
Statistical level ..	>0·001	>0·001	>0·001	>0·01	>0·01

Difference between P.M. and P.M. maximum also significant at an 0·01 level for both groups.

Table II gives all the intercorrelations of the different variables, so that the results for the two groups can be compared. In neither of the two groups is age correlated with any of the three intellectual estimates, a combined correlation

of the two groups remaining insignificant. It can be inferred, then, that the difference in age of the two groups does not directly account for the differences in intellectual ability indicated in Table I.

TABLE II

Intercorrelations of Variables for Both Groups

		Age	P.M.$_1$	P.M.$_2$	P.M. Maximum	M.H.V.S.
Age	Senile ..	−1180	+0227	−0545	*−5533*
	Depressed	−1931	−1694	−2365	−0517
P.M.$_1$			*+8764*	*+4639*	+1485
			+7023	*+7596*	*+6403*
P.M.$_2$				*+4971*	+0419
				+8081	*+6529*
P.M. maximum					+0669
					+5630

Correlations in italics are significant at a $>0{\cdot}01$ level.

What is apparent from Table II is the presence of a decline of verbal ability with age for the senile dementia group. It is presumably an effect of this decline that the usual positive correlation obtaining between intellectual and verbal ability is absent in the senile dementia group, although it is still present in the elderly depressed group. It would seem that while the depressives appear to be functioning like the normally aged, the seniles show a highly significant disruption of the ability to recall even the meanings of words used in everyday speech.

The comparatively low correlation between the Progressive Matrices scores and the computed maximum scores in the senile dementia group again indicates the effect of a marked function fluctuation of intellectual ability in this group relative to the depressed group.

With both groups it will be noted that even allowing for this fluctuant interference in performance, there is a definite inability to go on to the six most difficult problems of the test which demand a genesis of new material by the eduction of relations.

DISCUSSION OF INTELLECTUAL TEST RESULTS

The senile dementia group is distinctly older than the depressive group, indicating, at least as far as this sample is concerned, that senile dementia becomes more evident with advanced age than depression. The elimination of borderline cases from the sample may have resulted in the age difference being more clear than it is in fact.

In intellectual productivity, the senile dementia group is definitely poorer in output than the depressive group—a result which cannot be explained by the respective age differences owing to a lack of correlation here between age and intellectual productivity. This difference in intellectual productivity of the two groups is partly eliminated when allowance is made for fluctuation of performance. The difference in verbal ability which has been obtained between the two groups is perhaps a more basic factor, which itself determines this disturbance of intellectual productivity. Judging by their intellectual potential, the two groups are more comparable than in intellectual productivity, owing to the disturbance of the latter in senile dementia. As in younger age ranges, the verbal ability of the depressive group positively correlates with intellectual productivity. This correlation is absent in senile dementia, and this picture,

together with a decline of verbal ability with age, again indicates that the differentiating characteristic of senile dementia is to be found in verbal performance.

The progressive decline with age of verbal ability in senile dementia reflects a more profound disruption of the ability to direct and integrate mental activity, whether to solve problems or even to recall relevant information. This is what is apparent clinically in the dementing process of senility. If allowances could be made for the relative smallness of the age range and for the varying quality of acceptable vocabulary definitions, this decline of vocabulary would perhaps be even more apparent in the senile dementia group.

The disturbance of intellectual productivity, evidenced in its function fluctuation, is a result of this breakdown of organized mental activity in senile dementia. Invalid intellectual test performances which resulted in the omission of certain senile dementia patients from the group studied here can then be explained as being due to so great an interference with the smooth functioning of intellectual ability that no sustained performance is possible.

The preceding results suggest that in advanced age, the assumptions underlying present methods of assessing intellectual deterioration are questionable. If, as it would appear, the recall of acquired verbal ability itself breaks down in senile dementia, the assumption that verbal ability provides a measure of the best previous level of intellectual functioning no longer holds true in these cases. In fact, the decline of verbal ability, as indicated here, may prove to be a more direct measure of this disruption than disturbances of intellectual functioning.

Results (Rorschach Test)

Table III gives the details of those Rorschach variables found to differentiate the performances of the two groups from one another.

Table III

Rorschach Scoring Categories Found to be Different Between Seniles and Elderly Depressives at a $>0{\cdot}05$ Level

Category	Senile	Depressed
W percentage (Median)	40	28
Delayed response to the achromatic cards by ..	36% N	8% N
Shading responses given by	32% N	67% N
Anatomical responses given by	8% N	38% N
Inanimate movement responses given by	4% N	33% N
Form/Colour responses given by	28% N	71% N
Object responses mean percentage	24·9	12·6
Mean response time to VII (seconds)	11	22
Number of responses to X (total)	41	66

The Depressive Group

The deviations of the group are broadly in keeping with the Rorschach performances characteristic of younger age ranges of depression.

There is (1) a restriction of attention to detail responses, a trend opposite to the usual predominance of whole responses in normals of this age range; (2) the occurrence of shading responses is twice as great in the depressives as in the senile dementia group. These shading responses are equally composed of texture, chiaroscuro and achromatic types of response. They probably indicate the presence of introspective, anxious qualities which are relatively lacking in the senile dementia group; (3) Inanimate movement responses represent feelings of tension and are to be linked with (4) the greater incidence of anatomical

responses. These latter responses perhaps reflect concern and even hypochondriasis about the self, and may be connected with a difficulty in depressives of dealing with aggressive feelings and fears of consequent retaliation. (5) Compared with the senile dementia group, the depressives show more control over their emotional responsiveness to others, as indicated in the much greater incidence of form/colour responses. (6) The marked delay in responding to Card VII indicates shock to this card, and may again reflect depressive psychopathology. Philips and Smith (1953, p. 220), for example, interpret shock to this card as revealing extremely close, difficult and conflict-ridden relationships of the subjects concerned to their mothers. (7) The difference in the amount of response to Card X is difficult to interpret unless it indicates a greater potentiality for responding to the environment on the part of the depressives compared to the senile dementia group.

The Senile Dementia Group

The characteristic Rorschach features of the senile dementia group are mainly negative aspects of those obtaining for the depressive group. The relative absence of inanimate movement, anatomical and shading responses, indicate there is very little insight or awareness of any inner conflict. This absence of insight is perhaps reflected in (1) the greater incidence of delay in responsiveness to the achromatic cards. (This lack of insight or free anxiety is in keeping with the findings of other workers, who find virtually no shading responses in their senile subjects.) (2) The greater incidence of object responses seem to represent the lack of integrated biological impulses and a falling back on to static images of the material world.

The incidence of colour shock, poor form responses and organic signs was not found to be different at a statistical level of significance between the two groups.

Comparison of the Two Groups with Other Findings

Table IV gives a brief summary of the two groups reported here with the findings of other investigators on normal and abnormal old people.

TABLE IV

A Comparative Summary of Different Rorschach Findings

		Normals				Senile Dementia			
			Prados and Fried				Ames *et al.*		
Category	Depressed This Study	50–60	61–70	71–80	Ames *et al.* 70–100	Dorken and Kral	(early)	(marked)	This Study
Age	68·2					76·3	70–100	80	73·8
Number of Subjects	24	13	12	10	41	30	140	19	25
R ..	17·3	20	23	20	25·9	15·1	15·7	13·5	14·8
M ..	1·0	2·6	1·9	1·8	3·3	1·1	1·6	0·2	0·8
FM ..	2·5	4·8	5·0	5·1	2·7	2·8	2·0	0·3	2·1
m ..	0·3	0	0	0	0·7	0·1	0·3	0	0
FC ..	1·6	1·8	1·7	0·2	1·0	0·7	0·3	0	0·6
CF ..	0·5	1·5	1·6	0·2	1·3	0·4	0·5	0·2	0·2
C ..	0	0·2	0·2	0·3	0·2	0·2	0·1	0·1	0·2
EC ..	1·3	2·7	2·8	0·8	2·1	1·1	0·7	0·2	0·8
W% ..	31	61	52	43	36	31	43	46	42
D% ..	56	37	46	55	47	50	47	45	47
Dd% ..	2	2	2	2	15	17	9	8	2
F% ..	62	49	49	62	50	55	64	92	70

The senile dementia group performances are similar to those given in other reported senile dementia groups. They are similarly distinguished from the normal old age groups by their greater restriction, together with a marked intellectual and emotional impoverishment.

The depressive group in certain respects shows a similar restriction of response when compared with the relevant normal old age group, but these are features of the usual depressive record as previously discussed rather than the trend characteristic of senile dementia.

Conclusions

Studies with old people have often contained comments on the similarity of performance to that of children, not only in respect of intellectual ability, but also with regard to personality. The individual, with maturation, develops from childhood to maturity, and then in old age regresses back down the course of development. Ames *et al.* (1954), for example, find the most normal of their subjects respond like adults of younger age ranges—but with increasing deterioration, their Rorschach test performances come to resemble in many respects those of children. A similar comparison can be made from the present study of Rorschach test performances, and also in the average level of intellectual productivity, which is comparable to that of six year old children. In addition, the present study has shown that the modification of intellectual and verbal abilities in old age possesses important differences from those occurring in younger age ranges, and that verbal ability has begun to deteriorate. It would be unwise to overstress the "second childhood" aspects of old age, and so lose its particular characteristics and what faculties are retained or improved. Further studies are required, particularly longitudinal ones, to investigate precisely the changes of performance in normal old age and their relation to those changes occurring in both elderly depression and in senile dementia.

Summary

1. Tests of intellectual and verbal ability were administered to a group of senile dementia patients and to a group of elderly depressives, along with the Rorschach test.
2. Statistically significant differences were obtained from a comparison of the intellectual and verbal test performances of the two groups, and the variables concerned were intercorrelated.
3. There is a difference between the two groups of both intellectual productivity and intellectual potential, although the difference in potential is not nearly so marked as that of productivity due to the effects of fluctuation of performance on the latter.
4. A decline with age of verbal ability in the senile dementia group was demonstrated to be a more basic characteristic of senile dementia than disturbances of intellectual functioning, and will necessitate a modification of the concept of intellectual deterioration in advanced age.
5. Characteristic differences in Rorschach performance were obtained between the two groups, and a comparison made with other studies of old age and senile dementia.
6. The results of the present study are held to be of practical value in offering diagnostic aids in differentiating depression in old age from senile dementia.

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AN INVESTIGATION INTO THE VALUE OF "OBJECTIVE TEST PSYCHOTICISM" IN PREDICTING RESPONSE TO INSULIN COMA THERAPY*

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In spite of more than twenty years experience with insulin coma therapy psychiatric opinion as to its efficacy is by no means unanimous. While some recent large scale studies (Polonio and Slater, 1954; Paster and Holtzman, 1949; Barres, Ey and Laboucarie, 1953) point to a significant rise over the spontaneous recovery rate with the use of insulin, others (Jensen, 1952) do not find more than an acceleration of recovery already in process. Inasmuch as most investigators acknowledge an increased number of relapses in treated patients this latter view has some support. However the strongest case for insulin is that, if nothing else, it greatly reduces the patient's stay in hospital (Sargant and Slater, 1948; Hughes, 1951). If one remembers, however, the extra administrative and medical staff required to run an insulin ward this point is largely negated. In fact there are some (Bourne, 1953; Notkin *et al.*, 1939) who would claim that any improvement shown in insulin treated patients arises from the extra care and individual attention given them.

It would be possible then, as Bourne (1953) has in fact already done, to gather a formidable array of evidence from the literature suggesting that mental hospitals might well dispense with insulin treatment. However, until some objective method of selecting patients for insulin therapy becomes available we can never be sure whether the treatment itself is ineffective or whether it is simply being applied to the wrong patients. As Sargant (1949) has pointed out the initial success of Weir Mitchell's relaxation therapy led first to its wide adoption for many patients for whom it was unsuited and then to its rejection because it failed to cure them. Inasmuch as insulin therapy has suffered a similar rise in popularity it is possible that it too is being abused and that many of its failures are primarily the result of misapplication.

One would imagine that selection of patients for treatment would come through the medium of diagnosis and the statements that young early schizophrenics, perhaps with a certain amount of exogenous precipitatory stress, are most likely to respond to insulin summarizes the opinion of most texts on the subject. Yet, as Mayer-Gross (1951) and others point out, even with careful selection still around 40 per cent. of patients do not respond positively to treatment.

More important seems to be the diminishing confidence held in the traditional diagnostic classification system. For instance Harris (1950), Dorcus and Shaffer (1950), Sargant and Slater (1948), Cameron, Freeman and Stewart (1954) have all indicated the futility of diagnosis in determining the type of

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therapy a patient should receive. Perhaps the most pointed comment comes from Rees (1951), who, in discussing specifically the validity of diagnosis in selecting cases for insulin treatment remarks that,

> "I doubt very much whether the concept of schizophrenia has done anything to help us in choosing our cases. A diagnosis to have any value should give us (*a*) a clinical picture of the patient, (*b*) an indication of the course of the illness which would be helpful in giving a prognosis, and (*c*) some guidance as to the appropriate treatment for a particular patient. Most clinical psychiatrists will agree that the diagnostic label schizophrenia fails us in all these respects."

In this view, then, it is small wonder that insulin treatment has so many failures when it is given nowadays in many hospitals to patients who, somehow or other, have come to have the label of schizophrenia attached to them.

In addition to psychiatric opinion perhaps the most convincing evidence for the redundancy of diagnosis comes from the recent findings of Funkenstein *et al.* (1950) that successful response to E.C.T. can be predicted from blood pressure changes following epinephrine and mecholyl injections *independently of diagnosis* and that these changes are correlated with changes in abstract thinking ability, Meadow and Funkenstein (1952), Meadow *et al.* (1953). Other isolated findings showing predictive factors cutting across diagnosis can be found in the literature. Although there is not always agreement between them (cf. Kline and Tenney, 1951; Freudenberg, 1941, on body build) this only serves to emphasize the unreliability of psychiatric diagnosis, a point demonstrated by Ash (1949). It would seem clear then, that in choosing patients most likely to benefit from insulin therapy diagnosis is not a very satisfactory criterion.

Studies specifically designed to predict the outcome of insulin therapy are not hard to find. Recently Pascal and his students (1953, 1954a, 1954b, 1954c, 1954d) have examined exhaustively case history criteria correlated with prognosis but these studies have yet to be related specifically to any kind of treatment. Even so it is difficult to see how their findings can improve upon diagnosis for many of the factors under investigation like affective expression, orientation, direction of aggression, precipitatory stress, etc., are themselves subjective and are taken into account in arriving at a diagnosis. Of more concern to us are the investigations into the prognostic value of psychological tests and these fall into three major categories: studies of the Rorschach, the MMPI and miscellaneous objective cognitive tests.

The most prolific writer on the efficacy of the Rorschach in predicting response to insulin has been Piotrowski who, in a series of papers including (1938, 1941, 1952) has claimed success in predicting the outcome of insulin therapy from Rorschach signs. However, as Windle (1952) has already indicated, Piotrowski's signs change from paper to paper and serve mainly to show the failure of the empirically determined signs to stand up on cross validation. Other studies by Halpern (1940), Filmer Bennett (1952), and Rees and Jones (1951) also fail to point conclusively to any great prognostic value of the Rorschach. Of the MMPI studies Carp (1950b) has shown that patients who improved after insulin had higher pre-treatment scores on the F, Pt and Sc scales and lower scores on the K scale and Feldman (1951) has constructed an *ad hoc* scale predicting response to shock therapy in general. However it is difficult to obtain any theoretical lead from scales constructed from miscellaneous MMPI items although Carpenter (1953) has made such an attempt with the Feldman scale.

Studies using objective tests for prognostic purposes have been few and,

for the most part, unsystematic. The earliest of these, Bolles, Rosen and Landis (1938) found inferior performance on concept formation and sorting tests like those of Vigotsky and Weigl to suggest a poor prognosis with insulin therapy but this finding seems not to have been confirmed (Graham, 1940). Despite Carp's (1950a) indication that high pre-treatment Weschler IQ is favourable, in general intelligence test scores have not been found to have any consistent relation to response to insulin. However this and other inconsistencies may be due, as Zubin and Windle (1954) have pointed out to different degrees of chronicity in the patients examined. Windle and Hamwi (1953) taking this factor into account when attempting to predict response to surgical treatment did find that whereas superior performance on a complex reaction time test suggested good prognosis in illnesses of short duration the reverse was so for long standing illnesses.

Apart from the study by Pullen and Stagner (1953) on changes in rigidity following shock treatment little systematic work seems to have been done using objective tests either for predicting response to or measuring changes due to insulin therapy. Studies on lobotomy have been done by Crown (1952, 1953) and Petrie (1952) using objective test batteries factorially developed by Eysenck (1947, 1952a, 1952b) and it is with this type of test that we are concerned here.

Factor analysing a large battery of tests differentiating between normal and psychotic subjects Eysenck (1952a) claims to have established a personality factor of psychoticism. As insulin therapy has generally been thought to be applicable to patients recognized as psychotic subjectively it seems probable that selection of patients for insulin treatment on the more objective criterion of psychoticism as discovered by Eysenck would lead to improvement in the recovery rate. Thus we would predict that abnormal patients scoring within the normal range would not show recovery after insulin, and that the amount of recovery shown by patients scoring mildly psychotic would be greater than those shown to be severely so.

As our purpose is to attempt to rescue insulin treatment from rejection due to misapplication the distinction between spontaneous remission and that due to the effects of insulin is not important for the present. If we can succeed in first eliminating unsuitable patients from the treatment group then we may turn to the specific effects of insulin. Prior to this condition we can conclude nothing about the value of the therapy for if any group under investigation contains many unsuitable patients inevitably results will be poor. Only in well selected groups is it legitimate for the specific effects of insulin to be studied.

The Test Battery

From the tests described by Eysenck (1952a) differentiating significantly between normal and psychotic subjects the following tests were administered.

I. Expressive Movements

(a) *Waves*

The material consisted of a piece of squared paper with four V's, 1·5 cm. high on it. The V's were placed one above the other about 8 cm. apart. S was shown the first V and asked to trace over it. Then, with his eyes closed and arm and hand off the table S was asked to continue drawing six more V's along the same line. After finishing the first line S was guided to the next V and so on

until all four series were finished. In all cases the V's were covered as S drew them in case he should open his eyes.

Scores

1. Average amplitude in millimetres of the four first and four last waves.
2. Average length in millimetres of all the waves measured parallel to the edge of the paper.

(b) *Circles and Squares*

S was asked to draw first three circles and then three squares on plain sheets of paper.

Scores

3. Time in seconds to draw the circles.
4. Time in seconds to draw the squares.
5. Largest circle diameter in millimetres.
6. Largest square diagonal in millimetres.

II. Fluency

S was asked first to name as many birds as he could and then as many flowers as he could in 30 seconds. In this test Eysenck allowed 60 seconds but as on preliminary trials we found this time too long only half this time was given in this experiment.

Scores

7. Number of birds mentioned.
8. Number of flowers mentioned.

III. Mirror Drawing

The mirror drawing apparatus was placed in front of S and he was shown the paper with the numbers 1, 2, 3, 4 on it forming the corners of a diamond. After demonstrating that he must join the points 1 2 3 and 4 consecutively the paper was placed in the apparatus and S told that he must now join the points by looking through the mirror and that he must not remove his pencil from the paper until he had finished. The instructions were repeated until S was clear as to what his task was. We found, as did Eysenck, that constant re-assurance was necessary. The time to complete the task was recorded and reported to S. He was then asked to *estimate* his time for the second trial. On completion of the second trial S was asked to *judge* the time he had taken and to estimate his time for the third trial but no indication of the actual time taken was given. Altogether five trials were given, this is only half the number given by Eysenck but the task proved so difficult for our patients that it was found impracticable to continue beyond five trials.

Scores

9. Average time in seconds to complete one trial.
10. Average of the four judgments.
11. Average of the four estimates.

IV. Tapping

S was asked to tap with a pencil on a piece of paper. No reference was made to speed and in response to questions S was told that it was up to him.

Score

12. Number of taps in 15 seconds.

V. Reversal of Perspective

Our S's were shown the Necker cube and informed of the reversal phenomena. We did not, however, succeed in getting any of our earlier patients to experience the reversal. On replacing the cube by the more interesting Rubens vase we were still unable to demonstrate the ambiguity to the S's, and so the test was dropped from the battery.

Subjects and Administration

All patients other than re-admissions and recognized organics entering the Lebanon Hospital for Nervous and Mental Disorders during the early part of the summer of 1954 were tested within their first few days at the hospital. Testing was carried out without knowledge of and very often prior to psychiatric diagnosis. Similarly diagnosis and decisions for treatment were made in ignorance of the test results. Consequently test data was available on groups of patients (*a*) who were considered by the psychiatrists to benefit from insulin or shock treatment and (*b*) who were considered not likely to benefit from such treatment. Ideally we would have preferred both groups to undergo treatment in order to compare psychiatric judgment with test results. However in a practising hospital such a procedure is not feasible and consequently it is only possible to see if differences exist on the test battery between patients who responded and patients who did not respond to treatment after prior selection.

Altogether 25 patients who were tested were subsequently selected for insulin treatment and 9 of these received E.C.T. in addition. The patients' ages range from 15 to 45 years with a mean of 29 years and the group included 5 females. The battery of tests was usually completed in one session lasting about one hour.

Results

At the termination of therapy the patients were assessed by the staff psychiatrists to be either socially recovered, recovered, improved, unchanged or worse. Of these only the socially recovered patients were considered able to return to their pre-hospitalization position in society. Consequently it was decided to compare pre-treatment test scores of this group with the remaining patients. Nine patients were treated with E.C.T. as well as insulin and in order to avoid ambiguity the four patients recovering with the combined treatment were excluded from further analysis. The remaining five patients were included in the non-recovered group. This was considered justifiable for these patients received 37, 35, 18 and 26 insulin comas respectively and so could reasonably be judged as not having recovered with this treatment. The recovered and non-recovered groups had means of 30 comas and 25·8 comas respectively and their average ages were 29·2 and 30·2 years respectively. Neither of these differences is significant.

Table I shows the means and variances of the groups on the separate tests.

TABLE I

Pre-treatment Means and Variances of the Patients Rated Recovered and Non-recovered Immediately After the Termination of Treatment

		Recovered with Insulin			Not Recovered			
	Score	N	M	V	N	M	V	t
1	.. ..	9	19·77	28·17	12	17·17	13·31	NS
2	.. ..	9	102·4	1162·24	12	99·83	1010·14	NS
3	.. ..	9	24·22	237·50	10	39·20	2995·36	NS
4	.. ..	9	33·22	1218·16	10	35·20	2109·56	NS
5	.. ..	9	45·55	875·0	10	39·30	497·61	NS
6	.. ..	9	38·0	657·11	10	41·91	482·69	NS
7	.. ..	9	8·0	23·11	12	5·58	18·91	NS
8	.. ..	9	4·44	6·25	12	4·25	11·69	NS
9	.. ..	8	48·87	597·36	11	54·45	2932·79	NS
10	.. ..	8	69·13	3188·36	9	46·11	2950·99	NS
11	.. ..	8	83·87	2850·43	9	31·00	733·10	·05
12	.. ..	8	39·87	248·85	8	38·75	389·14	NS

On all scores except the first both groups scored as psychotic as Eysenck's (1952a) original patients and so may be regarded as being psychotic before treatment in this sense. Score number 11, the average of the estimated times for the four mirror drawing trials after the first is the only one to differentiate between the groups even at the ·05 level and may be regarded as a chance finding. None of the other scores even approaches significance.

As the battery as a whole is taken as a measure of psychoticism results on individual tests are subsidiary to those on the total battery. However the expected consistency in direction through all the test is not found for whereas scores 3, 4, 6, 7, 8, 9 and 12 show the recovered group to have been less psychotic before treatment than the non-recovered group scores 1, 2, 5, 10 and 11 show the reverse of this. Although it is probable that by weighting the individual tests according to their differentiating powers in the present analysis an *ad hoc* prognostic battery could be obtained it is equally likely that such a battery would not stand up to cross validation. Furthermore as it was our purpose to examine the prognostic ability of a battery of tests developed within a particular theoretical framework such *ad hoc* manipulation is inadmissible. We must conclude, then, that degree of psychoticism as objectively defined by Eysenck is no criterion against which to select patients for insulin therapy irrespective of whether our particular battery can be adjusted to be predictive or not. Whether this failure points to the non-specificity of insulin therapy or to the lack of validity of Eysenck's tests we are not at present able to say. In view of the general uncertainty as to the value of insulin treatment and the weight of evidence presented by Eysenck (1952b) in support of his tests as measures of psychoticism the more likely conclusion is that the effect of insulin therapy is not dependent upon the initial degree of psychoticism as used in the present sense.

SUMMARY

It was pointed out that before the effect of insulin shock treatment could be gauged effectively a method of selecting those patients to whom the treatment was appropriate needed to be devised. The common criterion for therapy, that of diagnosis, was shown to be inappropriate and the relative value of a few psychological tests was discussed. However the need was felt for a theoretically determined battery of tests to predict recovery with insulin rather than the generally unsystematic studies heretofore. The battery of tests used by Eysenck (1952b) to identify a factor of psychoticism was chosen as most promising and administered to a group of patients about to undergo insulin therapy. It was predicted that non-psychotic patients would show no improvement with insulin and that mild psychotics would improve more than severe cases. All the patients obtained high scores before treatment and so were

regarded as psychotic on this objective basis. However no consistent relationship between pre-treatment scores and degree of recovery was found; on half the tests the recovered group scored as less psychotic than the non-recovered group and on the other half more so.

It was concluded that either Eysenck's tests are not valid measures of psychoticism or that pre-treatment degree of psychosis is not predictive of response to insulin coma therapy.

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A CASE OF CHILDHOOD PELLAGRA WITH PSYCHOSIS

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PELLAGRA is a rare disease in Great Britain. The majority of cases occur among patients in mental hospitals and institutions (Stannus and Gibbons, 1934), and more recently it has been described as an accompaniment or complication of a chronic psychosis (Hardwick, 1946). Sporadic cases do arise in the general population (Davis and Hinden, 1941), but it is likely that in many instances the disease goes unrecognized (Deeny, 1942). Pellagra is particularly uncommon in British children (Greenfield and Holmes, 1939), although observers in areas where the disease is rife are of the opinion that it is found more frequently in children than in adults (Weston and Weston, 1948).

Mental symptoms are frequent in pellagra and may, in fact, precede the other manifestations (Sydenstricker, 1943). Severe psychoses occur in untreated cases and depressive, manic and paranoid reactions have been described (Hardwick, 1946). In children, however, symptoms are usually mild and mania or delirium is not often present (Holt and McIntosh, 1953); therefore this case of pellagra with a psychotic reaction in a 10-year-old English schoolboy may be of interest.

CASE REPORT

M.H., male, aged 10 years 8 months, was admitted to the Children's Department of the Maudsley Hospital in May, 1953. The history was of dermatitis of 5 months' duration and the sudden onset of severe mental disturbance 6 days prior to admission.

Family and Social History

The father, an unstable personality with a criminal record, deserted his wife soon after the patient's birth and the mother, a woman of low average intelligence, had experienced considerable difficulty keeping the family together. They had changed residence frequently and were at the present time in poor financial circumstances living in cramped quarters in a relative's house in South London. Three elder siblings were healthy with no history of nutritional disorder.

Personal History

The patient had lived in England all his life. Birth and early development were normal apart from "teething convulsions". At the age of 7 years he had spent 6 months in an institution because of housing difficulties, and had changed schools several times. A report from his present school described him as a slow but average scholar.

Previous Personality

Up till the age of 8 years he was described as active, friendly, obedient and rather submissive in his relationships with other children. On his return from the institution he was shy and fearful in company, lacked energy and initiative, slept poorly at night, awakening with frightening dreams, and became excessively dependent on his mother. Although more settled after a time, he remained anxious and inhibited.

Dietary History

The patient had been a finicky eater for many years, his mother being hard put to satisfy his tastes within the limits of her income. He would not eat fresh meat, fish or green vegetables, preferring tinned meats, spaghetti, tinned beans, potatoes and bread, and took only small amounts of milk. These likes and dislikes were confirmed in hospital, where he always left meat and green vegetables untouched unless supervised.

History of Illness

In February, 1952, he first developed a sunburn-like reddening of the skin over his face, back of neck, knees, backs of hands and wrists, the skin later becoming scaly and dark. This condition gradually cleared during the next 3–4 months, but he occasionally complained of stiffness in his legs and appeared unsteady on his feet at times. There was an episode of diarrhoea lasting 3 days in September, 1952. In January, 1953, his mother noticed that he was unusually irritable and morose, had a poor appetite, slept badly, and was less active at play, tending to keep to himself. In April, 1953, the dermatitis recurred. The boy was sensitive and anxious about his appearance, kept his hands in his pockets and asked, "Am I going mouldy?" He complained frequently of fatigue and aching and stiffness in his legs. Four days prior to the onset of mental symptoms he was brought home from school with the story that, while competing in a race, he seemed to lose control of his limbs and staggered about in an uncoordinated fashion. Six days prior to admission he became acutely ill with insomnia, frequent crying spells, restlessness, agitation, and demands not to be left alone. He expressed strange ideas: that there was an object inside his body, he was unable to taste his food, his neck was loose, his limbs had become skinny, his head felt empty and he could not think properly any more. His mother also stated that he seemed afraid to swallow his saliva for fear he would be poisoned, and accused his family of disliking him, blaming first his mother and later his brother for his condition.

Examination on Admission

The patient was of average height with sallow complexion and dark hair. Muscular development was normal and there was no evidence of marked weight loss, or clinical anaemia. Temperature was normal. The skin showed erythema with pigmentation and desquamation affecting the exposed areas, i.e. the cheeks, the back and sides of his neck, the backs of wrists and hands and encircling both knees. The areas were sharply defined from healthy skin, particularly on the neck and hands. (The patient was examined by Professor A. W. Woodruffe and Dr. L. Forman, who described the skin lesions as typical of pellagra.)

Tongue was moist and clean, and slightly reddened at the tip. No cheilosis, angular stomatitis, or other mucous membrane lesion was present.

Cardiovascular, respiratory and gastro-intestinal systems showed no clinical abnormality. Blood pressure 100 mm. systolic, 80 mm. diastolic. Pulse 90.

Nervous System

Bilateral nystagmoid jerkings were present on lateral gaze, but there was no other abnormality in the cranial nerves or special senses. Resistance to passive movement was increased in both lower limbs. Power and co-ordination were normal. All tendon reflexes were brisk but equal on both sides. Plantar responses were flexor. There was slight unsteadiness of gait. Accurate sensory testing was not possible but there appeared to be subjective impairment of sensation to cotton-wool and pin-prick over the hands and feet.

Mental State

He lay quietly in bed and took little interest in his surroundings. His expression was apprehensive, he responded slowly to instructions and appeared bewildered. He knew his name but was disorientated for time and place and was unable to recall events in the past few days. Simple tasks and calculations were poorly performed and attention and concentration soon waned. He did not talk spontaneously but answered questions shortly and in a whisper before resuming his fixed, anxious expression. When questioned about any changes in his body, he became very disturbed and began to weep, saying "I can't feel myself. My legs have gone skinny. My head is empty and I can't think about things like I used to." When asked what was wrong with him, he touched his thigh and abdomen and became very agitated, attempting to get out of bed in a confused fashion. After reassurance, he described how "a finger with yellow stuff on the tip touched my leg in the night. Now it's in my stomach and it's burning me inside." He stated that his family did not like him and were responsible for his illness because of something he had done. During the day he remained in a confused dream-like state interspersed with short periods of intense anxiety when he wept loudly and clutched his chest, crying "I can't breathe. My heart has stopped and I will die. My brain has gone soft." His agitation and confusion were most marked in the evenings. He urinated in his bed and on the floor and repeatedly tried to run out of the ward. He was observed one evening sitting bolt upright with a terrified expression as if afraid to move. He then began to weep and scream "Look out! It's there in the bed. It's the finger," and tried to run away.

Progress and Treatment

The patient took a full hospital diet and copious fluids, but tended to be constipated. He remained confused and agitated and the bizarre delusions and vivid hallucinations were constantly present. He was markedly disturbed at night requiring fairly heavy sedation.

Treatment was begun with an initial dose of nicotinic acid 200 mgm. by mouth followed by nicotinamide 100 mgm. T.I.D. He was given a high protein and carbohydrate diet supplemented with marmite and milk.

There was a conspicuous improvement within 48 hours. He was less agitated, more in

touch with his surroundings, and slept well without sedation. He no longer reacted so violently to his hallucinations and delusions and these cleared by the fourth day. Disorientation remained and he now appeared vague and apathetic. The neurological findings were unchanged.

The dermatitis improved rapidly, clearing completely within 14 days. By this time all signs of acute mental and neurological disturbance were absent and the picture emerged of a dull, polite boy with little interest or initiative, content to wander about alone or gaze vacantly into space. He was reluctant to discuss his symptoms, but realized he had been ill. He had no clear recollection of the delusions and hallucinations, describing them as "bad dreams". He later became more alert, sociable and active, and on discharge from hospital 3 months later was described as "back to normal". Advice was given to his mother on the preparation of a balanced diet and maintenance dose of nicotinamide and yeast tablets was prescribed.

Pathological Investigations

Haemoglobin 84 per cent. (13·1 gm.). Red blood corpuscles 5·1 million per c.mm. Packed cell volume 43 per cent. Mean corpuscular volume 84 cu. microns. Leucocytes 12,300 per c.mm. Polymorphs 77 per cent., lymphocytes 20 per cent., monocytes 3 per cent. Cells appeared normal on the stained film. Erythrocyte sedimentation rate 5 mm. fall in the first hour. Wassermann reaction—negative. Cerebrospinal fluid. Pressure 120 mm. water. No block. Cells: 1 lymphocyte per cu. mm. Protein 40 mgm. per 100 ml. Chlorides 760 mgm. per 100 ml. Sugar: normal. Pandy test—negative. Wassermann reaction—negative. Lange test—no change. Urine examination: no abnormality. Liver function tests: no abnormality. Serum proteins: total protein 6·8 gm. per 100 ml. Albumin 4·3 gm. per 100 ml. Globulin 2·5 gm. per 100 ml. Stool examination: no abnormality.

Biochemical Investigations

No porphyrins or urorosein were found in the urine. The urinary output of nicotinic acid, nicotinamide and N_1-methylnicotinamide was estimated (over a three-day period) in the patient and a normal control while on an identical standard diet. Nicotinamide 100 mgm. was then administered on each of three days and the estimation repeated. The values obtained did not establish any abnormality in the major known excretion products of nicotinic acid, thus indicating that a disturbance in absorption and metabolism of nicotinamide was not an aetiological factor in this case.

The patient's urine showed a high output of indican in 24-hour volume specimens, a finding which has been frequently observed in pellagra (Spies and Butt, 1947), but which appears to be of particular significance in this case (Rodnight and McIlwain).

Electroencephalographic Examination

The record showed a mild abnormality only during overbreathing as is sometimes seen in toxic conditions. There were no paroxysmal nor localizing features in the record.

Psychological Investigation

A full psychological investigation was carried out after recovery to determine evidence of residual intellectual impairment. The earlier test results when compared with the previous educational level were suggestive of deterioration. Scores on the Binet Form L. were: Mental Age: 7 years 2 months; I.Q. 67, and performance on memory items was particularly poor. The patient appeared vague and bewildered and the scores were not considered a reliable indication of "true" intellectual level. Successive test performances showed a gradual improvement and scores on a wide range of tests three months after recovery gave no evidence of impairment. Scores on the Binet Form M. were: Mental Age: 9 years 6 months; I.Q. 88, which was commensurate with school progress prior to illness.

Follow-up After Discharge

The family moved away from London in October, 1953, but the patient was kept under supervision by the local school medical officer. A year later he was reported to be quite well mentally and physically, the only symptoms since discharge from hospital being a short spell of diarrhoea at the end of the summer while he was without his maintenance dose of vitamin tablets. His school work was described as satisfactory.

Commentary

The aetiology of pellagra has been a source of speculation and discussion since the first occurrence of the disease in the eighteenth century (Chick, 1951). Pellagra is now considered to be a multiple deficiency disease with disturbed metabolic relationships involving nicotinic acid, pyridoxine, tryptophane and possibly protein and other members of the vitamin B complex (Bicknell and Prescott, 1953). The clinical signs of pellagra have been experimentally produced in man using diets low in nicotinamide and tryptophane supplemented with

other B vitamins (Goldsmith *et al.*, 1952). Tryptophane is a precursor of nicotinic acid and its administration leads to an increased excretion of nicotinic acid metabolites in normal subjects and pellagrins (Sarett and Goldsmith, 1949) and brings about healing of the lesions in pellagra (Vilter, Mueller and Bean, 1949). The importance of the protein content of the diet has long been appreciated, and the above relationship may explain the pellagra-preventive effects of foods low in nicotinic acid but rich in good protein (Goldsmith *et al.*, 1952).

The exact amounts of the different constituents of the patient's diet were difficult to determine. It may however be accepted from his clinical condition that M.H. (of 34 kg.) was obtaining adequate calories and protein from the foodstuffs listed in the dietary history. Thus he did not gain in weight whilst on a controlled and adequate diet in hospital. Tabulated data on such foodstuffs shows that a diet composed of them and yielding 2,500 cal./day and 70 gm. of protein is very unlikely to contain less nicotinamide than the accepted average requirement of 12 mgm./day. As vitamin requirements vary greatly in different individuals and, indeed, in the same individual from time to time as the result of growth, inherent metabolic pattern and physical activity, it is not easy to estimate needs or intake with any degree of accuracy. The requirements for some nutrients are dependent on other components in the diet and an insufficiency of one may affect the requirement and utilization of others (Yudkin, 1951). Thus the present symptoms of deficiency in nicotinic acid are most likely to have arisen through M.H.'s requirement for the substance being above the average.

It has been suggested that chronic partial deficiency of nicotinic acid lasting many months or years produces functional or biochemical disturbances which are relatively mild whereas complete or almost complete depletion rapidly produced, causes severe or even fatal functional disturbances (Sydenstricker, 1943). The course of the illness in this patient would seem to support this hypothesis. It is likely that a state of sub-clinical nicotinamide deficiency had existed for some time prior to the appearance of the dermatitis. The symptoms reported by his mother of irritability, insomnia, apprehension and fatigue, have been described as initial features of the disease in adults (Frostig and Spies, 1940) and in children (Spies and Butt, 1947). The acute mental disturbance occurred during the second appearance of the dermatitis and followed soon after an episode of strenuous physical activity. This additional stress appears to have further disturbed the already precarious balance between metabolic demands and dietary intake.

The clinical picture of pellagra in childhood varies in some respects from that in adults. Spies and Butt (1947) explain this difference by the fact that in the adult nutritional deficiencies affect mature tissues, whereas in children they are engrafted on tissues in the process of growth and development. The striking dissimilarity in environment also influences the symptomatology: the infant or child leading a sheltered existence compared with the active and exposed life of the adult. In children glossitis and mucous membrane lesions are usually mild (Weston and Weston, 1948). Violent gastro-intestinal symptoms are less frequent and constipation rather than diarrhoea may predominate (Holt and McIntosh, 1953). It is of interest that diarrhoea was a minor feature of this patient's illness and that mucous membrane lesions were confined to a mild glossitis.

The nervous system is less severely affected in children but cerebral symptoms are an integral part of the disease and are present to some extent in every fully developed case. In the milder cases the children are dull, irritable, emotionally labile, easily fatigued and may show lack of progress at school (Ford, 1953). In more severe cases there may be an apparent deterioration in intellectual

capacity, the formerly bright and intelligent child appearing backward or even mentally defective (Greenfield and Holmes, 1939).

Evidence of spinal cord involvement is found when the disease has been present for a year (Dodd, 1941). Tremor, ataxia, spasticity and increased reflexes with extensor plantar responses have been described. Histological examination showed degeneration in the spino-cerebellar tracts and severe involvement of motor cortex and basal ganglia (Greenfield and Holmes, 1939).

Psychotic reactions are unusual and few are reported in the literature. Hutchison and Paterson (1923) recorded a psychotic reaction in a ten-year-old girl with a history of pellagra of some years' duration. She was described as "childish" and nervous in the years prior to the appearance of the dermatitis. On admission to hospital she appeared mentally defective, was extremely emotional and unreasonable with hallucinations of sight and hearing. She believed an attempt was being made to poison her and that someone was trying to cut her throat at night. This case is of particular interest because of the similarity in certain respects to the one presented in this paper. In both instances the patients were the same age and the illness of more than a year's duration. Both presented paranoid delusions and terrifying visual hallucinations, noticeably worse at night—features noted by Kanner (1952) as characteristic in children with delirious reactions of infectious or toxic origin.

The mental symptoms in pellagra, unless of long standing, are usually reversible and are particularly responsive to treatment with nicotinamide. Nicotinic acid is a constituent of enzyme systems which are essential for carbohydrate metabolism. The energy of nervous tissue is largely derived from the metabolism of glucose and a break in this process results in a disturbance of cerebral function. Thus a metabolic disturbance has been suggested as the underlying cause of the disorder of consciousness, memory and perception which occurs in pellagra (Himwich, 1951).

Summary

A case of pellagra in childhood is described with particular reference to the occurrence of a confusional psychosis. A metabolic peculiarity resulting in an increased requirement for nicotinamide is postulated as a possible factor in the cause of the illness.

A satisfactory response to treatment with nicotinamide was obtained and psychological testing showed no evidence of mental deterioration.

Acknowledgments

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INDICANURIA AND THE PSYCHOSIS OF A PELLAGRIN

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Pellagra with marked mental symptoms in a boy of 10, was cured by nicotinamide (Hersov, 1955). The boy's diet prior to development of the pellagra did not however appear to have been deficient in nicotinic acid derivatives. The following studies were initiated in search for a metabolic peculiarity which might explain this.

Urinary Nicotinamide Metabolites

The subjects and procedure. Clinical details concerning the boy, M.H., have been reported by Hersov (1955). Symptoms possibly pellagrous had been evident between February and July, 1952 and again from April, 1953 until his admission to the Maudsley Hospital on 9 May, 1953. Nicotinamide at 100 mg./day was administered from 16 May, 1953 until discontinued for the present investigations on 9 June, 1953. Eleven days later, M.H. and a boy P.R. of similar age (Table I) were placed on the same reproducible mixed diet which was estimated to contain 10 mg. nicotinamide/day. They were not confined to bed. The whole urine for a period of three days, was collected in Winchesters containing 100 ml. glacial acetic acid and toluene.

During a second experimental period, immediately following the first, the boys were kept on the same diet to which was added 100 mg./day of nicotinamide. This dose of nicotinamide was based on Goldsmith's (1942) study of nicotinamide metabolism in adult pellagrins, when 300 mg./day was administered. The total urine during 3 days was collected as before.

Nicotinic acid and nicotinamide were determined according to Friedemann and Frazier (1950) after a 10-fold concentration of a sample, *in vacuo*. Of the original urine 1 ml. was diluted to 20 ml. and treated with activated charcoal and *N*-methylnicotinamide determined according to Huff and Perlzweig (1947).

Results. The findings with both subjects are quoted in Table I, together with some data from other workers. Those with M.H. are not unusual, nor do the differences between M.H. and P.R. appear unusual when considered in the light of investigations with other subjects. The metabolites determined necessarily represent only a small proportion of the subjects' total nicotinamide intake.

TABLE I

Nicotinic Acid Metabolites

Subject	Nicotinamide Administered (mg.)	Excreted: Nicotinic Acid and Nicotinamide (mg./72 hours)	Excreted: *N*-Methyl Nicotinamide (mg./72 hours)	Excreted: Recovered (Percentage of amount administered)
Section A				
M.H.	0	0·61	8·8	—
M.H.	3×100	0·46	16·3	2·5
P.R.	0	1·15	16·5	—
P.R.	3×100	1·66	21·0	1·7
Section B				
J, H and M: C ..	0	0·87	10·8	—
D	0	1·68	42·8	—
E ..	0	1·01	8·5	—
F ..	0	0·94	13·1	—
E and C: 1 ..	0	—	7·6	—
2 ..	0	—	6·7	—
3 ..	0	—	4·0	—

Section A: present investigations. *Section B:* J, H and M: Johnson, Hamilton and Mitchell (1945); E and C: Ellinger and Coulson (1944); in these investigations adults were studied and the excretion quoted is that for 24 hours.

IDENTIFICATION AND DETERMINATION OF A CHROMOGEN IN URINE FROM M.H.

During the preceding analyses, chromogens in the urine specimens were found to interfere with some of the determinations. Thus in estimating *N*-methylnicotinamide an extraneous green colour developed in acid acetone solutions, while acid aqueous solutions became pink.

Urinary pigments in pellagrins. Bodansky (1952) and Duncan (1947) survey observations of the excretion of both indole chromogens and porphyrin pigments in the urine of pellagrins. There has been some confusion between the two categories of pigment. Indicanuria without quantitative determination was reported by some earlier workers, as also was a precursor of urorosein. Beckh, Ellinger and Spies (1937) derived a red pigment from the urine of pellagrins which they considered to be coproporphyrin and regarded as of diagnostic value; its excretion was reported to be reduced by nicotinamide together with other signs of pellagra. Watson (1939) and Rimington, Holiday and Jope (1946) have however given evidence suggesting this and a pigment observed in sprue to be indirubin, an isomeride of indigo.

Characteristics of the pigment from M.H. The pigment was most simply formed by heating at 100° for a few minutes acidified specimens of the urine, for example after adding 1/10 vol. of conc. HCl. It was then reddish blue and could easily be extracted with chloroform or *n*-butanol. When extracted with chloroform and examined with a direct-vision spectroscope, its major band was clearly of somewhat longer wave-length than the D line, being about 6,000 Å. No absorption was seen around 5,500 Å, the position of the band of urorosein and porphyrins. A weaker band appeared at 5,300 Å. Tests for urorosein and porphyrins were negative. The main pigment was concluded to be indigo blue, derived from indican in M.H.'s urine.

Determination of indican. Sharlit's (1932) method was applied, using 2 ml. of a 1/20 dilution of the urine with thymol, potassium persulphate and trichloro-

acetic acid, and measuring the colour with a Hilger Spekker absorptiometer using a filter with maximum absorption at 550 mμ. As a standard an 0·96 per cent. w/v solution of anhydrous cobalt sulphate was used. The indican equivalent of this, calculated from Sharlit's data and confirmed approximately by ourselves was 10 μg. (final vol. 3 ml.).

Persistent Indicanuria in M.H. in Comparison with Other Subjects

A comparison between the urinary indican of M.H. and of P.R., in Table II, emphasizes the high, persistent level seen in M.H. It is to be noted that these observations commenced eight weeks after his pellagra had been terminated with nicotinamide. The high levels were maintained over the total period of detailed observation of a further eight weeks, and were also observed again four months later. The indicanuria now observed is therefore very different from the transitory excretion of chromogen described by Beckh, Ellinger and Spies (1937) during actual pellagra, when many bodily functions are disturbed; it may, rather, be constitutional.

Table II

Urinary Indican in M.H. and P.R. Consuming a Similar, Standard Diet

Date	Subject: M.H. Age: 10 years 8 months Weight: 5 st. 5 lb. Indican (mg./24 hours)	Subject: P.R. Age: 9 years Weight: 4 st. 8 lb. Indican (mg./24 hours)
16 July	—	44
18 July	233	51
21 July	280*	—
24 July	210*	—
29 July	268	—
5 August	200*	—
6 August	288	—
7 August	310	—

* Incomplete collection of urine: estimate based on creatinine output.

Normal levels of indican excretion in children do not appear to have been recorded, in spite of the many earlier observations on indicanuria referred to below. Levels in adults were reported (Sharlit, 1932) to be between 40 and 160 mg./24 hours, with a mean value of 100 mg. or about a third the average level observed in M.H. It was therefore decided to determine typical levels in children and these are presented in Fig. 1. We are greatly indebted to Dr. W. W. Payne of the Hospital for Sick Children, Great Ormond Street, for co-operation in providing these specimens.

A significant increase in daily excretion with age is to be seen. Excretion in M.H. is exceptionally high in comparison with all the 30 subjects examined.

Other Observations

The indican excreted is believed to originate from indole, itself derived from tryptophane. While this latter conversion has been suggested as taking place in the tissues of the body, a more clearly demonstrated source is from intestinal micro-organisms. It was accordingly attempted to modify the microbial flora in M.H. by administering succinyl sulphathiazole, 7·5 g. orally per day

for 7 days. No consistent change in indole excretion was apparent. Values before treatment were as indicated in Table II, that immediately preceding the sulphathiazole being 230 mg./day; during it, 215, 280, 255, 210, and following it 360 mg./day were excreted. Faecal examination showed a considerable preponderance of *Strep. faecalis* over coliform organisms during the treatment. Wooldridge, Mast and Hoffman (1950) have had similar experience with adult subjects.

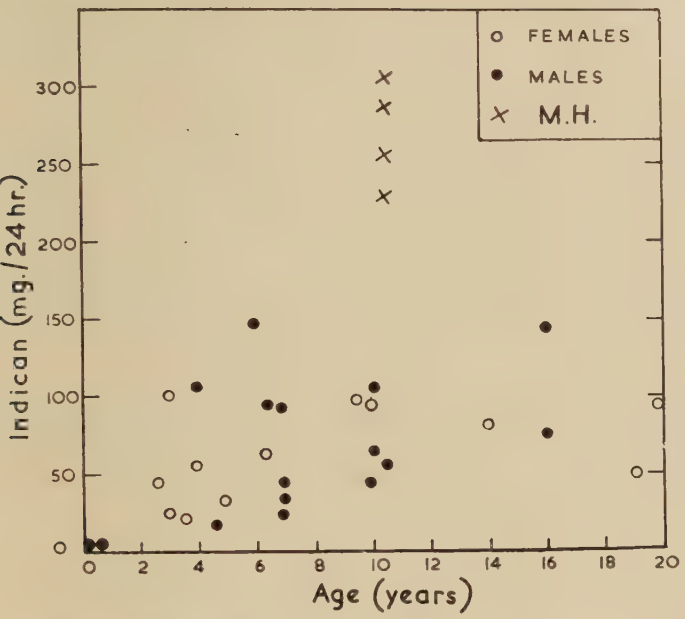

FIG. 1.—Urinary indican in male (●) and female (○) children and in M.H. (×).

A further experiment sought to modify his condition and the indicanuria by administering *l*-tryptophane, of which 1·5 g. (with 1 g. *D*-tryptophane) was given orally on two successive days, in two equal doses, as a suspension in blackcurrant puree. Indican remained at its usual high level (288, 310 mg./day) and observation showed no marked mental or physical change.

M.H. has not been accessible to us for further studies. A search, in which we have been aided by Dr. Denis Leigh and Dr. W. Hardwick, has revealed an adult case whose indicanuria and clinical history are similar to those of M.H., the indican again being much higher than that of her contemporaries. No other comparably high urinary indican has been observed in over 200 specimens. The studies are being continued.

DISCUSSION

Fifty to sixty years ago, indicanuria was regarded by several writers as a sign of "intestinal stasis and autointoxication" to which many disorders of the central nervous system were ascribed (Bouchard, 1894; Herter and Kendall, 1909). These suggestions were based on the hypothessis that indole or associated materials acted as toxic agents. Townsend (1905) reported instances of high indicanuria in depressed states and also in some maniacal phases, the severity of the mental disturbance varying with the elevation in indican output. Although general correlation of this type did not survive more critical examina-

tion (Folin, 1904; Segal, 1924), the present findings indicate that the psychosis of pellagra may be associated with a persistent indicanuria. After initial and often vague sensory, motor and emotional disturbances, the mental disorder of pellagra ordinarily has the appearance of a depressive or manic-depressive illness (Justin-Besançon and Lwoff, 1942). Pellagra has a long association with mental hospitals (Medical Research Council, 1930; Reiter and Jacobsen, 1935; Justin-Besançon and Lwoff, 1942; Caldwell and Hardwick, 1944; Leigh, 1952) and as its mental symptoms may occur before other indications of the disorder they may not always be recognized as part of a deficiency disease. Pellagra was indeed regarded as a microbial disorder in the 1890s, as also was the auto-intoxication.

Moreover, recent observations suggest a basis for association between nicotinamide deficiency and indicanuria, for tryptophane can serve as precursor not only of indican but also of nicotinamide sufficient for half the daily requirement of this substance. Thus indicanuria may represent a diversion of tryptophane from a more essential metabolic route, making an individual more exacting in his requirements for dietary nicotinamide. It is possible that these metabolic conversions take place in the body rather than or as well as occurring in the intestinal contents. Another important route from tryptophane leads to serotonin.

Greater nutritional needs in pellagrins in mental hospitals were envisaged by Reiter and Jacobsen (1935). Requirements for a given dietary essential can differ in individuals by a factor of 5 or more (Williams, Eakin, Beerstecher and Shive, 1950) indicating individual metabolic pecularities of which indicanuria offers a relevant example. Granted that the "normal" requirement for a vitamin is the mean or mode of a distribution curve, the extreme requirements can be understood in a large population to differ considerably. Very many metabolic and other processes are involved between the assimilation of foods containing nicotinamide and tryptophane, and the functioning of the coenzymes derived from either of these substances. It is presumably variation in such processes in different individuals which leads to requirements for nicotinamide which are higher or lower than usual. We suggest that indicanuria represents one group of processes leading to high nicotinamide requirement and thus an especial proneness to pellagra.

This study does not indicate new therapeutic measures other than that sympathetic consideration be given to peculiar feeding habits, for these may not only be the cause of some nutritional disorders but may in other instances be in part protective, as is anorexia in thiamine-deficient rats.

Summary

1. A boy who developed pellagra with marked mental disturbance on an apparently normal diet, did not show unusual quantities of urinary nicotinic acid, nicotinamide or *N*-methylnicotinamide on an ordinary diet nor on one supplemented with additional nicotinamide.

2. He showed unusually high persistent indicanuria, excreting about 280 mg./day of indican.

3. A survey of indicanuria in children indicated the average excretion to increase with age, the value in the boy's contemporaries being less than 100 mg./day.

4. Whereas indicanuria has in the past been thought to be connected with mental disorder through the toxic action of indole or associated materials, it is now suggested that such connection can be due to a diversion of tryptophane metabolism from more essential routes.

Acknowledgments

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A NOTE ON URINARY COPPER-REDUCING STEROID EXCRETION IN PATIENTS WITH PSYCHIATRIC DISORDERS

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Introduction

Altered adrenocortical activity has been reported in patients suffering from primarily psychiatric disorders by Hemphill and Reiss (1947), Reiss, Hemphill, Gordon and Cook (1949a and b) and others. The chance finding of a high urinary copper-reducing steroid (CRS) excretion in a man suffering from recurrent depressive illnesses who was suspected of having Addison's Disease, prompted us to investigate the excretion of these steroids in a group of unselected psychiatric patients. We report here the results of 23 estimations on 21 patients.

Methods

Twenty-four hour urine collections were made. The CRS content was estimated after benzene-water partition by the method of Talbot, Saltzman, Wixom and Wolfe (1945), within 2 hours of the completion of the collection. Normal results by this method are 0·1 to 0·4 mgm. per 24 hours (Talbot *et al.*, 1945).

Results

The results of the estimations are shown in the Table. In 8 of the 21 patients the CRS excretion was abnormally high. Follow-up of these patients revealed that at one year Case 14 had committed suicide; Case 15 was not well, and Case 16 could not be traced. Five years later Cases 17 and 18 were well; Case 19 was suffering from Paget's Disease; Case 20 was improved but not well, and Case 21 was a certified schizophrenic in a mental hospital.

Discussion

The technique of Talbot *et al.* (1945) estimates at least some of the unconjugated metabolites of the adrenocortical hormones which are excreted in the urine. The method was criticized by Marrian (1951) on the grounds that it was not specific for this group of steroids. More recently, however, de Courcy and Gray (1953) examined the method and concluded that it gives results "which although high, approximate more closely to the probable amount of adrenocortical hormones present". Brooksbank, Owen and Prunty (1950) showed that the urinary CRS measured by this method increased after stimulation of the adrenal cortex by A.C.T.H.

TABLE

No.	Sex	Age	Presenting Symptom	Urinary Reducing Steroid Excretion in mg. per 24 hours	Clinical Follow-up
1	M	43	Depression	0·25	Improved at 1 year
2	F	52	Depression	0·22	Relapsed at 1 year
3	F	28	Anorexia	0·18	Well at 1 year
4	F	51	Headache	0·27	Not followed up
5	M	60	Generalized prurigo with lichenification ..	0·23	Unchanged at 1 year
6	F	61	Recurrent depression ..	0·23	Not followed up
7	M	63	Noises in head	0·06 0·32 after 8 E.C.T.	Worse at 1 year
8	M	60	Depression	0·15	Died 2 years later
9	F	50	Depression	0·13	Unchanged at 1 year
10	M	60	Depression	0·17	Worse at 1 year
11	M	41	Alcoholism	0·23	Unchanged at 1 year
12	F	17	Urticaria, angio-neurotic oedema ..	0·12	Well 5 years later
13	F	31	Anxiety	0·23	Not improved at 1 year
14	F	50	Hypochondriasis ..	0·91	Suicide 9 months later
15	M	26	Abdominal pain ..	0·79	Subsequently developed duodenal ulcer; not well at 1 year
16	M	25	Depression	0·52	Not followed up
17	M	54	Recurrent depression ..	2·43 1·53 after 2 weeks in hospital	Well 5 years later
18	M	54	Suicidal depression ..	0·74	Well 5 years later
19	F	46	Headache	0·66	Not well 5 years later: Paget's disease of spine and femur
20	F	51	Anxiety	1·02	Improved 5 years later
21	F	23	Drug addiction	2·35	Certified mental hospital patient 5 years later

There have been many reports of psychiatric disorders in patients suffering from adrenal virilism with increased urinary 17-ketosteroid excretion (Broster, Allen, Vines, Patterson, Greenwood, Marrian and Butler, 1938; Allen, Broster, Vines, Patterson, Greenwood, Marrian and Butler, 1939; Allen and Broster, 1945; Greene, Paterson and Pile, 1945). The mental condition of these patients improved after successful treatment of the virilism. However, this need not imply, as has been sometimes assumed, that the mental state is organically related to the physical condition. None of the female patients in our series had physical signs of virilism.

Seeking for an explanation of the increased CRS excretion in 8 of our patients, the only feature of the psychiatric condition common to them was the greater degree of anxiety which they exhibited compared with those patients in whom the CRS excretion was normal. The most severely disturbed patient, Case 21, showed the second highest CRS excretion. Five years later she is still in a mental hospital. This is of interest in view of the subjective sensation of intense anxiety reported by Bray, Merivale and Willcox (1952) during ephedrine medication, which in their subjects was accompanied by a marked increase in CRS excretion.

Summary

Increased urinary copper-reducing steroid excretion was observed in 8 out of 21 patients suffering from a variety of psychiatric disorders. These 8 patients evidenced greater anxiety than those in whom the CRS excretion was normal. This finding suggests that emotional factors can alter the values obtained in such estimations, and this must be borne in mind when the test is used for the evaluation of organic disease.

Acknowledgments

We thank Dr. T. A. Munro, lately Director of York Clinic, Guy's Hospital, for his interest in this investigation, and for allowing us access to his patients; also Dr. J. H. Watkin, Physician Superintendent of Horton Hospital, for allowing us to see Case 21.

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CLINICAL BLOOD-PRESSURE IN ANXIETY

By

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THAT variations of blood-pressure are found in states of emotion is commonplace knowledge; that rises may take place with temporary fear and anxiety is also well known, but that anxiety occurs with a reduced or normal blood-pressure is not perhaps so well appreciated.

The purpose of the present investigation was to determine whether the blood-pressure remains high when the patient with anxiety is in a state of overt placidity and calmness.

METHOD

By recording, under similar conditions, the blood-pressure of cases with overt anxiety and of those without, comparison of findings can be made with a control series. In this investigation, the 310 subjects investigated were female in-patients admitted to a nursing home, those without diagnosed anxiety forming the control series. No selection of cases was made.

TECHNIQUE

The blood-pressure readings were recorded by one observer, the writer, by means of the auscultatory method, a mercurial manometer being used. The systolic and diastolic pressures were taken more than once, the process being continued, without removal of the armlet, until the lowest level had been attained. The recordings were made with the patients lying supine in bed on the morning following their admissions to Mount Pleasant, a nursing home for psychiatric cases. The patients were in bed from the time of admission until after the blood-pressure recording, a period varying from 17 to 24 hours.

Tables I and II show that the mean systolic pressures were, although not statistically significantly so, in each age-group lower amongst the cases showing overt anxiety than in those not showing it. The mean diastolic pressures, although again the differences are not statistically significant, do not show this difference in each age-group, being lower only in the age-groups 70–79 and 80–89 years.

In no case of any age-group was the maximum systolic pressure higher amongst the anxiety cases than amongst those not showing this condition.

TABLE I

Systolic Pressures

Series	No Anxiety	Anxiety	No Anxiety	Anxiety	No Anxiety	Anxiety	No Anxiety	Anxiety
Ages	10–59		60–69		70–79		80–89	
No.	33	97	18	27	32	43	37	23
Mean	131·0	117·9	162·0	159·9	161·3	145·3	154·8	149·96
S.E.	±4·41	±2·76	±8·28	±6·35	±5·83	±4·04	±5·93	±5·88
S.D.	25·33	27·17	35·11	33·01	32·99	26·50	36·04	28·21
Range	92–240	80–200	94–225	100–210	115–230	90–230	90–240	110–240

TABLE II

Diastolic Pressures

Series	No Anxiety	Anxiety	No Anxiety	Anxiety	No Anxiety	Anxiety	No Anxiety	Anxiety
Ages ..	10–59		60–69		70–79		80–89	
No. ..	33	97	18	27	32	43	37	23
Mean ..	76·9	82·8	86·87	93·50	87·4	82·4	100·6	83·7
S.E. ..	±3·95	±1·63	±4·35	±3·14	±2·98	±2·52	±4·11	±3·24
S.D. ..	22·69	16·08	18·52	16·32	16·84	16·54	24·98	15·55
Range ..	40–150	32–170	60–142	60–125	60–120	40–130	60–150	50–110

The maximum diastolic readings did not show this same difference in each age-group. The cases without overt anxiety showed greater variability than those with it, as in all age-groups the S.D.s of the systolic and diastolic readings were greater amongst the cases without anxiety, although in the age-group of 70–79 years, diastolic, the difference is slight.

Psychoneurotics under stress conditions have been shown by Malmo and Shagass (1952) to show consistently higher systolic pressures than normal controls. Consequently, the lower mean pressures of the anxiety cases in this investigation is evidence of the patients being under no direct stress situation at the time of the recordings.

The possibility exists that amongst the cases of this investigation which showed no overt anxiety symptoms, anxiety was nevertheless present. Dogs, during early training, although apparently without fear, have been shown to have very high blood-pressures (Wilhelmj *et al.*, 1953), although later in training the pressure falls. Although these dogs showed no signs of apprehension if strangers entered the laboratory, marked and approximately equal rises of systolic and diastolic pressures occurred. The more highly trained dogs showed much greater blood-pressure responses to trivial environmental changes than did those less well trained. Wilhelmj and his co-workers suggest that frequent daily repetitions of emotional states over years may lead to persistent elevation of blood-pressure, and that the degree of restraint and conditioning characteristic of the average person may produce a state of irritability of the vasomotor centres, so that minor tensions may lead to hypertensive states. Although the last part of this sentence could be regarded as confirmed by the present investigation as regards the systolic pressure, it tending to be higher in those persons not showing overt signs of anxiety, the first part is certainly not so confirmed. The patients who were undergoing emotional reactions of an anxiety type did not show higher systolic readings, and in only two age-groups did they show higher diastolic records.

This investigation appears to show definitely that overt anxiety does not produce a hypertensive state which persists during periods of placidity.

SUMMARY

The systolic and diastolic pressures were recorded under standard clinical conditions in 120 females not showing overt anxiety and in 190 females showing this state. All were relatively calm externally at the time of examination.

The means of the control series and of the anxiety cases showed no statistical differences in any age-group from 10 to 89 years, but in each age-group the means of the systolic pressures of the anxiety cases were lower than those of the control series. The means of the diastolic pressures did not show this relationship in two of the four age-groups.

Overt anxiety did not produce a state of hypertension persisting during periods of placidity.

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Reviews

Clinical Psychiatry. By WILLIAM MAYER-GROSS, M.D., F.R.C.P., ELIOT SLATER, M.A., M.D., F.R.C.P., D.P.M., and MARTIN ROTH, M.D., M.R.C.P., D.P.M. Cassell & Co. Ltd., London, 1954. Pp. 652+xvii, 16 plates. Price 50*s*.

This is a consolidated, up-to-date presentation of clinical psychiatry, expounded by three clinicians of diverse experience who share a leaning towards research and an unshakable conviction that psychiatry is and should remain inherent in medicine itself, and should eschew esoteric cults and excessive expansionist movements.

In it, the authors have incorporated most of the worthwhile advances in knowledge that have accrued from the researches of many workers (for which they provide an abundant bibliography) in the past twenty-five years, especially in such matters as the incidence, genetics and physical pathology and treatment of psychiatric illnesses.

One of the authors' main aims is to discern in the simplest form those factors which are essential, or pathogenic, as distinct from those which are incidental, or pathoplastic, in producing various attributes of personality and various syndromes. By contrast with the psychobiological school, they emphasize the similarities among various groups of mentally sick or disabled persons, and rank the differences in the unique histories of such individuals as of secondary importance. From this is derived their concept of a "multi-dimensional approach"—the search for various dimensions in which the actions and reactions, the gifts and handicaps of the individual, and the symptoms of various illnesses to which he may be heir, can be compared, and if possible measured, by reference to standard scales.

In the main, the presentation of the subject matches the authors' attitudes and fulfils their intention. Clinical descriptions of, for instance, the major psychoses and the marginal territory that is shared by neurology and psychiatry, are vividly realistic and impeccably correct. The psychoneuroses and psychopathies are dealt with together in one chapter, as if they were regarded, after the fashion of some continental schools, as not very clear-cut variants of only a very few fundamental deviations of personality. Here, as elsewhere in the book, advice about management and treatment, including psychological treatment, is unexceptionable, though in some respects rather at variance with the impression one gets from the authors' views about psychology and psychotherapy in an earlier chapter, in which they review briefly the major schools of psychiatric thought.

In their preliminary remarks they have, too, some hard things to say about the British psychiatrists of a generation or two ago. Many will think these unwarranted and likely to serve little purpose in furthering the instructional aims of the book: indeed, the reader might be forgiven for wondering, at some points, whether the authors have not been in some danger of partisanship in some of the familiarly contentious parts of the psychiatric field, which would be a transgression of their own ostensible standards of dispassionate objectivity.

With the exception of the chapter on psychoneuroses and psychopathies, the arrangement of the book is conventional; but little is said about psychosomatic disorders, and in relation to drug addictions there is a valuable exposition of pharmacology applied to psychiatry. In addition to material already mentioned, there are sections on case-taking, mental deficiency, psychiatric disorders of children and the aged and on legal and administrative psychiatry. The latter ranges rather diffusely through a comparative study of concepts and procedures in various countries. It is unfortunate that there are one or two slips—for instance, a reference to temporary "certificates" (sic), when one of the main purposes of temporary treatment is the avoidance of certification; and it is not correct to suggest that the practitioner approved for making the necessary recommendations in this matter must be a specialist.

The plates are unusually abundant for a modern textbook of psychiatry, and although of excellent quality and great interest so far as they illustrate, for instance,

somatotypes and neuropathology, it is not easy to see the necessity for depicting, in a book of this relatively advanced class, the apraxia for dressing in a case of Pick's Disease or the postures of schizophrenics.

It would be excessively sanguine to expect that the first edition of such a massive work as this, from the pens of several authors, would be entirely free from points of criticism; but its positive and constructive qualities far outweigh any imperfections there may be. No one could doubt that this is a sincere, valuable and reliable work, conceived in the disciplines of medicine itself and presented in a clear and most instructive form. It is unquestionably a major contribution to British psychiatric literature, and in addition to its instructional purposes, for which it is suited particularly to the needs of the specialist in training, it is a valuable basic work of reference for those who contemplate research in the clinical field.

IAN SKOTTOWE.

Prenatal Psychology. By M. LIETAERT PEERBOLTE. A. W. Sijthoff, Leyden, 1954. Pp. 182. Price D.Fl.15.

Dr. Peerbolte has considerable difficulty in distinguishing fact from fiction, memory from phantasy. It was to the very great credit of Freud's genius that he was not unduly discouraged when the "memories" of his patients were found on occasion to be phantasies: the important point being that it is the patient's mind that is being examined; and it is an important fact that the patient's mind produces phantasies.

But Dr. Peerbolte spoils his fascinating case by interpreting his material as the memory of prenatal experiences, rather than as the adult phantasy of prenatal existence. Thus Dr. Peerbolte says, "Of course it is possible that retrojection of postnatal ideas" was responsible for a certain patient's dream but the dream's characteristics "indicate a prenatal experience".

There is something disquieting about a prenatal psychology which avers that it is possible to remember being part of one's mother's ovary, to remember being born as an ovum, followed by the "shock" of fertilization, to remember being thereafter a personality developing in the womb. One has grave doubts whether in fact one has memories of intrauterine "traumatic events", such as the partial displacement of the placenta, or the father's penis in the vagina. Some of the so-called "facts" of intrauterine life are most dubious—thus "the original knowledge of the mother about her ovum is transferred to the egg itself after or during conception"; and "the fact that in prenatal psychology emotional life is localized in the fetus and the recording apparatus, or centre of the personality, in the placenta".

Dr. Peerbolte sometimes regards all this as phantasy, but more often as fact capable of being remembered. A certain patient during analysis "showed spontaneous fits of lowered consciousness which were accepted by the analyst as deep regressions into her inner self". In such a state she said, "I should like to pray that I may not be condemned to remain an ovum in all eternity, let me come into existence." Very well, the fact is she said that. After waking up from another such state of mind she said "I felt very near to God, but this is not possible; I nearly re-experienced my own conception; there was some holy ghost hovering over it, but one cannot summon this ghost". Again, one accepts that that was what she said and it was evidently of great import to her; no less so, were one to believe it to be phantasy. But Dr. Peerbolte says "The analyst could reply: it is not a question of summoning, it is only a question of recollecting."

One does not doubt that "prenatal occurrences can influence postnatal life", but one should be extremely cautious about believing one can recollect these experiences; and one doubts very much whether psychotherapy could influence to that depth behaviour modified by such early experiences. On the contrary the immense human interest, conscious and unconscious, in sex may be expected to give ample impetus for phantasies regarding conception and prenatal life. Notwithstanding Dr. Peerbolte's claims, it is from this point of view of phantasy that the material of this book may be expected to be of most value. One can more readily modify adult phantasies.

It is to be noted that the patient, who was dwelling on conception, was using religious terms: in this book there abound ideas of extrasensorial perception, of death and resurrection, of infinity and cosmic feelings, of re-incarnation and re-birth. It is to be hoped that prenatal psychology, having to concern itself with such notions, will contribute to a deeper understanding of religion than psychology has hitherto accomplished.

It is also of interest that prenatal psychology has material comparable to the animus and anima of Jung. It is refreshing to find points of contact between the different schools of psychology.

Dr. Peerbolte regards prenatal psychology as an extension of Freud's work and makes the important claim that prenatal psychology can treat cases "not well accessible to Freudian psychoanalysis"; these include "prepsychotic states and states of depersonalization". It is also stated "the author has not yet found any age-limit for prenatal analysis, . . . he even analysed a patient aged 59". In contrast also to Freudian psychology, the emphasis of Dr. Peerbolte's prenatal psychology is on the woman; "in dreams spermatozoons happenings are never recorded". One feels that neither of these extreme views, of the relative importance of either sex, has the ring of balanced truth.

The Dutch author is to be congratulated on his remarkably good English; and he writes quite modestly, for example he admits, in discussion of a certain point, "the ultimate root has so far escaped us". He repeatedly acknowledges his debt to Dr. Nandor Fodor, to whom the book is dedicated.

C. E. H. Turner.

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Insulin Coma Therapy in Schizophrenia

1. Insulin coma therapy at the Pennsylvania Hospital produced an immediate improvement or remission in 67·7 per cent. of 780 patients treated between 1936 and 1951.

2. At least 334 patients, or 63·3 per cent. of all patients who originally improved, had a relapse; 44 per cent. of all these relapses occurred within 30 days, and 78 per cent. within one year of treatment. A second insulin course brought about an improvement or remission in 52 per cent. of 122 patients who had relapsed.

3. Factors associated with the most favorable prognosis include: age over 16, psychosis of less than 6 months' duration, with a clinical picture of paranoid, catatonic, or undifferentiated schizophrenia; and if during treatment the patient receives at least 30 to 60 coma hours and gains more than 30 pounds in weight.

4. They conclude that insulin coma therapy is effective in restoring the schizophrenic patient to his prepsychotic adjustment. This restoration to health is not accompanied by a permanent correction of the factors that predispose the patient to regress to schizophrenia.

(Authors' Abstr.)

The EEG Changes in Unilateral and Bilateral Frontal Lobotomy

1. In cases of unilateral and bilateral frontal lobotomy, temporal slow wave activity was found to be a prominent feature, though more transient than the dominant frontal slowing. This non-frontal slowing may be interpreted as the result of cerebral edema and hippocampal herniation from operative manipulation.

2. There is an apparent correlation between the degree of slow activity in the postoperative EEG and clinical improvement, in that slight or severe degrees of slowing was found to be more conspicuous in those cases that exhibited little clinical improvement. In contrast, moderate slowing was associated with moderate to marked clinical improvement.

3. The frontal slow wave activity, though decreasing in prominence, persists in the majority of cases for at least 3 years and possibly longer.

(Authors' Abstr.)

The Effect of Adrenochrome and Niacin on the Electroencephalogram of Epileptics

1. Adrenochrome in dosages of 10 mgms. does not change the EEG of normal volunteers, but in 10, 25, and 50 mgm. doses increases the bilateral paroxysmal abnormalities in the EEG of epileptics, but has very little effect on the cortical focus itself.

2. Nicotinic acid given orally or intravenously in normal volunteers showed a slight shift in EEG frequency to the fast side; in epileptics the drug considerably decreases the bilateral diffuse paroxysmal abnormalities (except in true idiopathic epilepsy), but has very little influence on the focus itself.

3. The mode of action of the above-named drugs is discussed.

4. A tentative explanation is offered as to the genesis of the paroxysmal EEG disturbance in schizophrenia.

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The Limbic System ("Visceral Brain") and Emotional Behavior

Experimentation of the last 15 years suggests that the limbic system, which anatomically is a common denominator in the brains of all mammals, is also, physiologically speaking, a common denominator of a variety of viscerosomatic and emotional reactions. In this paper, especial attention is given to the recent developments pertaining to the part of the limbic

system contained in the hippocampal formation. Bioelectrical studies are cited that provide further evidence that this part of the brain is afferently related to all the sensory systems. From these and other experiments concerned with ablation and stimulation, inferences are derived that give additional support to the theory that this region of the brain is concerned with the experience and elaboration of emotion.

(Author's Abstr.)

Amino Acids of the Cerebrospinal Fluid

The procedure for the identification and quantitative estimation of the free amino acids of the cerebrospinal fluid, using ascending two-dimensional paper chromatography, is given in detail.

Average losses during the procedure have been determined.

Spinal fluids from 26 surgical patients with no evidence of neurological disease have been analyzed by this procedure and compared with fluids from 12 well-authenticated cases of multiple sclerosis.

No significant quantitative difference, or any consistent qualitative difference, characterizes the amino acid pattern of the multiple sclerosis group.

Proline and methionine were identified in a small percentage of the fluids studied which contained red cells, but in no other fluids.

(Authors' Abstr.)

Studies on Headache

Eight persons subject to vascular headache of the migraine type had technically satisfactory studies made before, during, and after 26 headache attacks, with the following results:

1. Decreased rates of excretion of water, sodium, potassium, and creatinine were usually observed prior to and during the early phases of vascular headache of the migraine type.
2. Increased rates of excretion of water, sodium, and potassium were usual with subsidence of the headache attacks.
3. Creatinine excretion returned to "normal" values during subsidence of headache, with four exceptions. On these four occasions potassium excretion was high.
4. Weight gain prior to the headache attack was common but not invariable. It sometimes occurred well in advance (7 to 10 days) of the onset of headache.
5. Weight loss with subsidence of headache was usual. However it was sometimes delayed 24 to 48 hours.

It is concluded that the described fluid, electrolyte, and renal changes are not causally or mechanistically related to the onset, intensity, or duration of the migraine attack. Instead, they are manifestations of the widespread bodily changes accompanying adaptive reactions during and after stressful periods. The migraine attack is a concurrent, but independent, feature.

(Authors' Abstr.)

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Blood Platelets in Disseminated Sclerosis

In disseminated sclerosis the permanent changes are localized along the blood vessels, being associated with venules and veins. Histological examination of fresh foci do not reveal serious thrombotic changes, but often clots of blood platelets are seen in the central veins. In the present work the blood platelets in the circulating blood were examined with a view to variations in their number. The blood analyses were as far as possible extended over a fairly long period, as a rule up to one month, and in a single case six months. The values obtained were compared with corresponding values from a control and a normal series. In "stationary" disseminated sclerosis the authors found moderate fluctuations of the blood platelet number, somewhat greater than in the normal and the control series. During clinical activity there was a tendency to a low level, followed by a rise during improvement. The fluctuations proved to be considerably greater in patients with acute disseminated sclerosis than in patients with the stationary form or in normals, or in patients with other neurological disorders.

In principle, the curves run a similar course during infectious diseases and after tissue destruction, operations, etc. An increased tendency to agglutination is possibly also reflected in the blood platelet system.

The counts showed, furthermore, that in normals the variations in blood platelet number are much greater from subject to subject than from day to day in one subject.

Though the series under review does not allow of a simple comparison between the individual variations of the thrombocyte counts in patients with active and in patients with inactive disseminated sclerosis, the tendency toward a greater variability in the active group is so conspicuous that this question merits more thorough investigation.

(Authors' Abstr.)

Visual and Motor Instability in Multiple Sclerosis

In a fairly large group of patients with multiple sclerosis subjected to a standardized stress, the majority, or about 75 per cent., showed aggravation of symptoms, in some cases even considerable. The exacerbation occurred within 10 to 15 minutes. After the experiment was stopped, most patients returned to the status quo within 15 to 20 minutes, while others required a somewhat longer readjustment.

The symptoms apparently comprise the entire nervous system, including the visual function. Certain findings indicate that the visual impairment at least is not merely a nervous phenomenon, but that far more peripheral tissue changes may contribute. It is possible, but not yet proved, that peripheral changes also play a role in eliciting the other symptoms. Such a peripheral factor cannot be ruled out primarily in the frequently marked adynamia, which sometimes may be accentuated to total paralysis and may be characterized by features reminding one of myasthenia, e.g. ptosis, bulbar symptoms, hypotonia, and loss of tendon reflexes. Since, however, other signs were unmistakably of "central" origin—appearance of the Babinski toe sign and spontaneous nystagmus—it must be presumed that the clinical phenomena represent a widespread action upon the entire organism.

Heating of the nature described is a "stress" on the multiple sclerosis organism. It is well known that many multiple sclerosis patients have observed such exacerbations upon varied forms of stress, not the least by heating. The patients often report this spontaneously. These spontaneous statements were the very reason why the authors decided to investigate this aspect. Infectious diseases also aggravate the condition of sclerosis patients. Perhaps fever is the most important factor other than phenomena of more complicated nature, such as allergization.

In the experiments, unlike natural stress of spontaneous occurrence, the stress could be regulated and interrupted. Therefore, it has exerted its action within an extremely limited period.

As is well known, the physiological reaction to stress is a complicated one. Many factors are involved. As regards heating, they know that heating is the immediate cause of vascular dilation in the skin and in the central nervous system. The latter effect is known from a large number of animal experiments. Recently, Engel demonstrated such vascular dilatation also in the nervous system of man. This is, of course, of particular interest in connection with the present investigation, because various workers have shown that the pathological changes in multiple sclerosis are of perivenous localization. From the pathoanatomical point of view, multiple sclerosis is a kind of periphlebitis in which large plaques are formed by the confluence of numerous, small periphlebitic zones. It has been shown also that in fresh zones the dilated vessels are surrounded by edema. Marius Haarr (1951) has observed edema in the walls of the retinal vessels in multiple sclerosis.

The possibility of any development of edema in the parenchyma of the central nervous system must, however, be ruled out in the present experiments, considering that the symptoms subside in about 20 minutes. At any rate, such edema would have to be limited to the interstitial tissue. At the present time, it seems most reasonable to assume that an alteration takes place in the ion distribution in the membranes of the nervous system, of the eye and possibly of the neuromuscular apparatus, with a corresponding alteration in the membrane potentials.

The preliminary result of the present investigation is the finding that a certain proportion of patients with multiple sclerosis exhibit intermittent visual impairment which does not seem to be related to alterations in the optic nerve function. This impairment is elicited particularly by physical exertion or heat and may be induced or reproduced by exposing the patients to a certain degree of heating. Patients with multiple sclerosis present an abnormally high incidence of myopia, differing significantly from that in a Danish normal series. Lastly, fluctuations in the visual acuity are far commoner in myopic than in emmetropic or hypermetropic subjects.

(Authors' Abstr.)

Intravenous Hydrocortisone, Corticotropin and the Electroencephalogram

The intravenous administration of both corticotropin and hydrocortisone may induce an increase in theta activity (5 to 7 c/sec.) in the electroencephalogram, although hydrocortisone would seem to exert this effect more consistently and to a greater degree than does corticotropin.

The effect was somewhat greater in epileptic subjects with previously abnormal electroencephalograms. In two instances hydrocortisone produced an increased incidence of 2 to 3 c/sec. spike-wave seizure discharges.

Hydrocortisone produced essentially no change in serum sodium or chloride concentrations but did cause a significant elevation in serum potassium in five of the seven subjects studied. The electroencephalographic changes in these subjects could not be correlated with this electrolyte shift.

Corticotropin induced changes in the electroencephalogram in a patient with a functionally inactive adrenal cortex, suggesting that it may have a direct effect upon cerebral electrical activity.

(Authors' Abstr.)

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Clinical Experience with Meratran

1. The pharmacology of a new central nervous system stimulant, Meratran, is reviewed briefly.

2. The therapeutic indications of this compound are roughly similar to those of the amphetamines.

3. It has benefited the group of narcoleptic patients studied.

4. The drug continues to prove of value in reactive depressions.

5. In institutionalized patients its use is advised in non-deluded schizophrenics having restriction of interest and depressive features, in long-term schizophrenics with deterioration, and in cases of psychomotor retardation with blocking of communication. In patients with active delusions, anxiety, and agitated behavior it is contraindicated.

6. In geriatric practice the depressed but otherwise organically fit older patient who cannot be inspired to continue normal activities can be helped by small doses of the drug.

7. Numerous other clinical conditions, ranging from drug-induced lethargy caused by anticonvulsants, antihistamines, chlorpromazine, rauwolfia compounds, etc., to "afternoon letdown", alcoholic hangover, the fatigue and depression encountered in diabetes, parkinsonism, and hepatitis, etc. have been benefited by the employment of small doses of Meratran, according to various investigators.

8. Selected cases of blepharospasm and spasmodic torticollis have been helped by this drug. Other patients of this type cannot tolerate the drug in therapeutically effective doses. The effect of Meratran in stammerers is being studied.

9. The drug has proved valuable in office practice because the appetite loss and the cardiovascular pressor reactions sometimes observed after the administration of the amphetamines are not encountered. In addition, the drug seldom interferes with nocturnal sleep, and when it produces anxiety side reactions these are less severe and less disturbing subjectively than those encountered with the amphetamines.

10. When anxiety or agitation comprise a sizable proportion of the clinical picture the drug should be used warily and with caution.

11. Effective dosage ranges (except in narcolepsy and motor tics) vary between 2·0 and 25·0 mg. daily.

12. The drug appears to be a true central nervous stimulant without effect on the autonomic nervous system, and therefore is not a member of the sympathomimetic group of compounds. Experimental evidence at this time points to the reticular formation of the upper brain stem and/or the septal area as the primary site of action of the drug.

13. Initial observations on other compounds closely related to Meratran chemically indicate that they may open up new avenues of investigation in the field of neuropharmacology.

(Author's Abstr.)

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Electroencephalograms During Cycles of Addiction to Barbiturates in Man

1. The clinical and electroencephalographic changes which occur during chronic secobarbital intoxication and after abrupt withdrawal of this drug were studied experimentally in two groups of former narcotic addicts without previous histories of epilepsy or psychosis: group I, consisting of 14 individuals receiving 0·9 to 2·6 g. daily in divided doses for 33–89 days, and group II, including 21 individuals receiving 0·6 to 0·8 g. of the same drug for 38–58 days.

2. During the period of chronic intoxication, the subjects in group I displayed varying degrees of ataxia, dysarthria and other changes resembling those of cerebellar dysfunction, as well as marked changes in affect, sensorium and judgment. Concomitantly, electroencephalograms were characterized by mixed rhythmic fast and slow abnormalities, mainly in frontal and parietal tracings. Tolerance developed to the clinical effects of barbiturates, but not to the electroencephalographic effects. After abrupt withdrawal of barbiturates, varying degrees of anxiety, tremulousness, postural faintness, anorexia, insomnia, and weight loss developed in almost all the subjects. In addition, 79 per cent. exhibited 1–4 generalized convulsions on the second or third day of abstinence, and 65 per cent. displayed psychoses, generally in the form of agitated delirium, between the 4th and 7th day of abstinence. Concomitantly, marked changes appeared in the majority of electroencephalograms, generally in the direction of periodic hypersynchronization, and with the frequent appearance of mixed spike and slow wave or 4 c/sec. "spike-and-dome" paroxysmal discharges. After the 8th day, clinical recovery proceeded uneventfully, and electroencephalograms assumed a normal pattern in the majority of cases, with only mild abnormalities in the remainder.

3. During the period of chronic intoxication, the subjects in group II displayed mild or no evidence of ataxia, etc. Concomitantly electroencephalograms were characterized by predominance of rhythmic fast activity in the frontal and parietal tracings. After abrupt withdrawal of barbiturates, abstinence phenomena were similar to but much milder than those observed in group I. Only 2 subjects exhibited seizures, and none developed psychosis. In general, concomitant alterations in the electroencephalograms were similar to but milder than those in group I, with two striking exceptions. In these, paroxysmal discharges were more common than in any record obtained in group I. Clinical recovery proceeded uneventfully, while electroencephalograms assumed normal patterns in about half of the group, with mild random abnormalities in the remainder.

4. No one-to-one correlations could be demonstrated between any given clinical state and any given electroencephalographic pattern. However, the occurrence of clinical seizures was most commonly associated with random spike, diffusely slow or paroxysmal activity in electroencephalograms, and slow abnormalities of various sorts predominated during periods of psychosis.

5. The electroencephalographic changes occurring during cycles of addiction to barbiturates are discussed with reference to possible neurophysiological mechanisms.

(Authors' Abstr.)

Studies of the Electroencephalogram of Normal Children: Comparison of Visual and Automatic Frequency Analyses

Electroencephalograms of 71 normal children in one-year age groups ranging from 1 to 10 years inclusive were recorded. In all instances right and left parieto-occipital recordings were subjected to frequency analysis by means of the Ediswan Walter analyser. The results of the analysis, presented in the form of a scattergram for each one-year age group, show (1) relative constancy (under basic conditions) of frequency analysis of one area and similarity of homologous areas; (2) great variability of analysis within single age groups; this has been illustrated by electroencephalograms representative of relatively mature (fast) and immature (slow) patterns in each age group; and (3) evidence of individuality of delta (1 to 3 c/sec.), theta (4 to 7 c/sec.) and alpha (8 to 12 c/sec.) which undergo complex changes with development.

Four subjects (5·6 per cent.) had grossly abnormal tracings. While 3 of these subjects had focal sharp-wave discharges, the fourth had a diffuse abnormality. Of the 3 subjects with focal sharp waves in their electroencephalograms, 2 had normal records 18 months later. It is concluded that sharp-wave foci in children may have a less serious prognostic significance than in adults.

The relative merits of visual and automatic analysis are discussed together with suggestions for the practical application of automatic analysis in pediatric electroencephalography. It is suggested that combination of the automatic-analyser tracing and the 8 traces of the standard recording may result in reaching or even exceeding the threshold of data saturation of the observer. Such a situation may require compromises aimed at simplifying the final presentation.

(Authors' Abstr.)

The Use of Frequency Analysis in the Interpretation of the EEGs of Patients with Psychological Disorders

1. A method of using frequency analysis of the rates of EEG wave forms has been described which appears to produce consistent and useful results.

2. This method, used in conjunction with EEG interpretation and with psychological data has demonstrated positive correlations between EEG pattern and psychological factors which appear to confirm and to establish more firmly the observations of previous authors. They are of clinical diagnostic use.

3. In the present study a comparison was made among three groups: patients in a mental hospital; inmates of a prison farm; and control "normals". EEG data and frequency analysis showed significant differences in the three groups.

4. These differences showed a more exact correlation with psychological criteria produced by the various tests given. In particular, anxiety and aggression were each factors related to specific EEG patterns.

(Authors' Abstr.)

Metrazol and Combined Photic-Metrazol Activated Electroencephalography in Epileptic, Schizophrenic, Psychoneurotic and Psychopathic Patients

1. Photic, Metrazol, and combined photic-Metrazol activation was carried out in 47 epileptic, 20 psychoneurotic, 30 psychopathic, and 53 schizophrenic patients.

2. Combined photic-Metrazol activation was found to be a valuable and easily controlled method for the demonstration of low myoclonic thresholds in 84 per cent. of patients with idiopathic epilepsy, and in 53 per cent. of schizophrenics. A low threshold was obtained in only 2 per cent. of patients with psychoneurosis and character disorder.

3. The pattern of EEG response is different in epileptic and non-epileptic patients.

4. Combined photic-Metrazol activation has definite diagnostic value as an aid in the evaluation of patients with suspected epilepsy.

5. Electro-shock treatment has the immediate effect of raising the myoclonic threshold in schizophrenic patients, but the effect is a temporary one.

(Authors' Abstr.)

Studies in the Processes of Aging: Electroencephalographic Findings in 400 Elderly Subjects

1. Electroencephalograms were obtained on 400 subjects over the age of 60 as part of a project dealing with aging of the central nervous system.

2. One hundred senile patients, without evidence of gross focal neurological disease revealed that 22 per cent. had normal records with a preponderance of diffuse and mixed abnormalities.

3. In 145 volunteers from the community without neurological disease, a high percentage of focal disturbances were found, and a gradient of decreasing EEG abnormality of all types was noted with higher socio-economic levels. Focal disturbances alone did not seem to cause psychological impairment.

4. Psychological test data correlate diffuse and mixed EEG abnormalities with the greatest degree of psychological deterioration.

5. Forty-five psychiatric patients with no evidence of brain damage revealed patterns of electroencephalographic abnormalities similar to the community group of volunteers, 60 per cent. of their records being normal. Diffuse fast wave disturbances were relatively more frequent among the abnormalities seen.

6. Ninety-four neurological cases showed the expected low incidence in normal records and a heavy preponderance of focal disturbances.

7. A gradient of decreasing normal records was noted in progressively older decades. Diffuse dysrhythmias which followed this trend were due to slow wave disturbances. The incidence of focal records did not appear to change in succeeding decades, but a definite increase in the proportion of severe foci was noted in progressively older decades.

8. Diffuse fast wave disturbances were not frequent, and showed a tendency to decrease in older patients, as did the proportion of severe fast disturbances. No fast wave abnormalities were seen in patients over the age of 79.

9. The high incidence of foci in this series could not alone be correlated with psychological test evidence of deterioration. When foci were associated with diffuse abnormalities, however, organic deterioration was definitely noted. Primarily left temporal foci were often clinically silent. The suggestion was made that hippocampal degenerations or beginning generalized vascular disease might be the cause.

10. It was suggested that temporal foci could be more easily elicited using the vertex as a reference electrode, as well as keeping the ears "untied" and ungrounded. Also important was the use of the low-lying anterior temporal lead.

(Authors' Abstr.)

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Neurosecretory Pathways Between the Hypothalamic Paraventricular Nucleus and the Neurohypophysis

A description is given of the neurosecretory pathways between the hypothalamic paraventricular nucleus and the neurohypophysis in dogs, as observed in serial sections stained following the chrome-alum-hematoxylin phloxine procedure.

The area traversed by the principal mass of neurosecretory fibers corresponds to that occupied by Greving's tractus paraventricularis cinereus.

Two additional neurosecretory pathways are described which are parts of the paraventriculo-hypophysial system. Both originate in the caudodorsal tip of the paraventricular nucleus.

One of these accessory bundles extends into the lateral hypothalamic area where it is found in relation to scattered nerve cells exhibiting neurosecretory phenomena. The bundle turns medialward, dorsal to the supraoptic nucleus, and joins the supraoptic-hypophysial tract.

The other bundle provides the shortest and most medial, direct, connection between the paraventricular nucleus and the neurohypophysis. After looping over the fornix, first dorsal then lateral, it crosses the substantia grisea centralis diagonally and enters the infundibular separate from and caudal to the supraoptic-hypophysial tract.

Search for evidence of termination of the fibers among the cells of the supraoptic nucleus was unsuccessful. It is concluded, therefore, that the fibers arising from the paraventricular nucleus and associated with neurosecretory material for the most part establish a direct connection of the paraventricular nucleus with the neurohypophysis.

(Author's Abstr.)

The Anatomy of the Primate Brachium Conjunctivum and Associated Structures

1. The brachium conjunctivum is composed of three limbs—the well-known crossed ascending limb, the less well-known descending limb (crossed) and the hithertofore unknown uncrossed ascending limb.

2. No myelinated uncrossed descending limb exists.

3. The first and third of these three limbs are distributed to the ventrolateral part of the thalamus and globus pallidus of their respective sides. The pallidal contribution, although previously postulated, is hardly known to most students of the cerebellum.

4. The crossed ascending limb traverses the region of the red nucleus.

5. The uncrossed does not but it does enter the arcuate nucleus which it probably penetrates to end in the ventrolateral part of the thalamus.

6. The brachium conjunctivum sends no myelinated fibers to the subthalamic nucleus and there does not appear to be any notable contribution to the substantia nigra.

7. Fibers travelling with the crossed ascending limb do, however, arise from the red nucleus and pass to the subthalamic nucleus.

8. The descending limb sends fibers to the superior central, reticulo-tegmental and magnocellular reticular nuclei of the pontine region, enters the cervical spinal cord and may send some fibers to the opposite side of this.

9. The descending limb contributes to the medial longitudinal fasciculus.

10. The brachium conjunctivum may also, according to another supplementary plan, be divided into three components: dorsal, intermediate and ventral.

11. The uncrossed ascending limb arises more particularly from the dorsal component and the descending limb from the dorsal and intermediate components.

12. While all components probably contribute to the crossed ascending limb those elements arising from the dorsal and intermediate components send relatively more fibers to the thalamus than to the globus pallidus whereas the reverse situation is true for those elements arising from the ventral component.

13. The contribution of the dorsal component to the crossed ascending limb traverses, most particularly, the dorsolateral part of the area of the red nucleus, the ventral traverses the ventromedial area and the intermediate component the central area.

14. The arrangements and relations of the limbs and components of the brachium conjunctivum have been described in the text and a plan has been presented for the purpose of enabling the investigator to determine what parts of the brachium will be rendered nonfunctional as the result of a lesion in any part of it.

15. The mammillary peduncle arises from the deep tegmental nucleus of Gudden, ascends between the interpeduncular nucleus and substantia nigra and enters the lateral mammillary nucleus.

16. No specific, independent ascending mammillo-penduncular tract appears to exist apart from the mammillary peduncle.

17. The pallido-interpeduncular system appears to be a pallido-nigric system in large part.

18. The dorsal supraoptic decussation arises from, or in close proximity to, the medial longitudinal fasciculus.

19. The ventral supraoptic decussation arises from the dorsomedial portion of the mesencephalic tegmentum.

20. The reader's attention is called to the fact that the correlation between the anatomic material and the physiologic circumstances which transpired is reported in Carrea and Mettler (1955). (Author's Abstr.)

Observations on the Intracortical Relations of the Climbing Fibers of the Cerebellum

The climbing fiber has been found to possess more extensive synaptic relations in the cerebellar cortex than previously believed.

1. At the level of the Purkinje cell bodies recurrent collaterals are seen to disappear into the neuropil plexus of the granule cell layer. The synaptic relations of this collateral are not known.

2. Some collaterals are observed to make contacts with adjacent Purkinje cell bodies or their primary and secondary dendrites.

3. Collaterals and terminals have been traced to stellate and basket cell somata and dendrites where they appear to make synaptic contacts via boutons-en-passage or end feet.

4. Ascending and descending collaterals of the axons of stellate cells and basket cells are observed to effect axon to axon contacts with the climbing fibers. Such contacts are effected by typical end feet, boutons-en-passage, or through complex inter-twining of the elements.

6. The climbing fiber has also been observed to establish contact by means of its collaterals with the dendrites of large short-axoned stellate cells of the granule layer and with parallel fibers.

7. The stellate and basket cells of the molecular layer appear to establish synaptic contact with each other forming neuronal chains of varying lengths. Recurrent axonal collaterals have been traced back to the cell of origin. Collaterals of stellate cell axons are also seen to terminate by end boutons or ring forms on Purkinje dendrites.

8. It is suggested that a series of feed backs from various stages of the intracortical pathways, i.e. recurrent collaterals of the climbing fiber, of the Purkinje cell axon, and the axon of the large stellate cells of the granule layer form a plexus which may regulate the threshold of this receptive layer.

9. On the basis of the fine structure of the climbing fiber and the synaptic relations which they have just reported, it appears that this fiber activates a group of neuronal chains of varying lengths. Most of these chains seem to form closed loops with collaterals so arranged that activation of efferent units may occur simultaneously with reactivation of the chain. Maximum activation of stellate chains probably occurs in the immediate vicinity of the climbing fiber.

10. Available neurohistological and neurophysiological data suggest that the climbing fiber and the elements it activates may be responsible at least in part for the phenomenon of cerebellar localization. The hypothetical nature of this suggestion and the need for electrophysiological elucidation are stressed. (Author's Abstr.)

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pH of Cerebral Cortex during Induced Convulsions

1. The pH of the cerebral cortex was measured with membranes and capillary glass electrodes, and correlated with changes in cortical electrical activity induced by asphyxia, CO_2, Metrazol and nitrogen mustard.

2. During Metrazol seizures, cortical pH declined from approximately 7·3 to 7·0, and was neither preceded nor followed by an alkaline shift.

3. Acute asphyxia caused a fall of pH from 7·3 to 7·1. Hyperventilation produced a rise from 7·3 to 7·45.

4. Inhalation of 30 per cent. CO_2—70 per cent. O_2 during Metrazol seizure caused a fall of pH to 6·4 Metrazol discharge disappeared at pH 6·9 and reappeared at 6·7 when CO_2 inhalation was discontinued.

5. Nitrogen mustard seizure activity did not appear until after the cortex had been made acid (pH 6·6) by CO_2 inhalation, and the CO_2 then discontinued.

6. The implications of these findings are briefly discussed. (Authors' Abstr.)

Effect of Bilateral Ablation of Cingulate Area on Behaviour of Cats

1. In cats, bilateral ablation of the cingulate area in the frontal lobe produces a syndrome characterized by confused, perseverative, obsessive behaviour, and a plastic tendency whereby the animal may be posed for long periods of time in bizarre positions.

2. There is also evidence of change in emotional status such that rage reactions are more easily elicited.

3. This syndrome does not appear following removal of any other cerebral cortical area but it is intensified and prolonged by the additional removal of the frontal poles or of additional tissue from the mesial surface of the frontal poles.

4. Bilateral ablation of the motor areas, although it abolishes placing and hopping responses and results in consequent postural disability, does not produce the confusional and plastic condition which follows bilateral ablation of the cingulate areas.

5. The syndrome which follows bilateral cingulate ablation is similar to that described by Barris in 1937.

6. This syndrome has also some of the elements of postural confusion and of apraxia described in man following similar lesions. It is suggested that the hypomotility and inertia described by others in man and monkey as related to cingulate ablation may be the result of some motor element or dyspraxia. (Author's Abstr.)

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Variations in the Basophilia of Nerve Cells Associated with Increased Cell Activity and Functional Stress

After staining nerve cells with gallocyaninchromalum, a quantitative and stoicheiometrical staining reaction for nucleic acids, the cell pictures exhibit marked changes with variations in the functional and pathological activity of the cells. These changes consist in variations in the basophilia of the cytoplasm, nucleus, nucleolus, and nuclear membrane, accompanied by alterations in the form of the cell body and nucleus, and size of the nucleolus, as well as characteristic changes in the distribution of the basophilic elements in the cytoplasm and displacement of the nucleus inside the cell body. The fundamental cell stages of basophilia (chromoneutrality, hyperchromasia, chromophobia, chromophilia) are described.

Spontaneous variations in the basic staining reaction of the nerve cells constantly occur in the central nervous systems of normal animals and man, but are greatly enhanced by experimental procedures or in disease.

Chromophobia in certain human cases of patho-functional stress (acute delirium, death from convulsant treatment, traumatic epilepsy), as well as in the ganglion cells of Aplysia after electric stimulation is described.

All the evidence indicates that the cell pictures of chromophobia are to be interpreted as structural correlates of increased activity and abnormal neuronal discharge. Certain characteristic cell pictures provide strong evidence in support of the theory (Einarson, 1933, 1935) that the nucleic acid of the cytoplasm is formed primarily round the nucleolus inside the nucleus and then diffuses through the nuclear membrane to become a constituent of the basophilic elements in the cytoplasm.

(Authors' Abstr.)

Unusually Severe Lesions in the Brain Following Status Epilepticus

The case has been described of a boy who at the age of 9 became ill with Still's syndrome. In the course of this illness he suddenly went into status epilepticus, which was followed by three days' coma and pneumonia. On recovery from the acute episode he was found to be demented. Subsequently he had grand mal, petit mal, and also what may be described as temporal lobe seizures. He died 12 months after the first epileptic seizure.

At necropsy he showed widespread damage in the brain due mainly to circulatory and anoxic disturbances associated with the first status epilepticus. The lesions were most severe in the first temporal convolution and adjacent Sylvian regions. Ammon's horn and the hippocampal gyrus, the medial orbital and the anterior cingular regions. The amygdaloid nucleus showed extensive incomplete softening.

The pathogenesis and functional significance of the lesions are discussed. Particular attention is drawn to the combination of lesions in the first temporal convolution and hippocampus, which Earle, Baldwin and Penfield regarded as specific to herniation and anoxia at birth.

Special reference is made to the involvement of the amygdaloid nucleus.

(Authors' Abstr.)

Prefrontal Leucotomy and the Anticipation of Pain

In order to test the hypothesis that prefrontal leucotomy relieves painful conditions by reducing the anticipatory element of fear a pain-expectancy test was devised. The relative disturbance caused by a painful shock and by a preceding warning light was estimated by measuring the ratio of the psychogalvanic responses aroused by these two stimuli. Twelve of the 13 patients examined showed post-operatively an increase in this ratio which indicates a relative reduction in the autonomic disturbance caused by the warning signal. It was shown that this reduction in the anticipatory fear associated with a painful stimulus was not due to an alteration in the perception of pain or to a reduction in the amount of pain tolerated during the test.

One subject, who had been relieved by leucotomy of a totally incapacitating preoccupation with a post-herpetic neuralgia, is reported in detail.

(Authors' Abstr.)

Intellectual Changes Following Temporal Lobectomy for Psychomotor Epilepsy

Testing of patients undergoing temporal lobectomy for psychomotor epilepsy suggests that following the operation:

1. General intelligence is relatively unimpaired.
2. Specific abilities may be impaired, at least for some time.
3. A significant learning disability may result.
4. The disability is strongly associated with lesions of the dominant hemisphere.
5. The disability may still be present a year after operation.
6. The learning disability is not a function of the level of intelligence of the patient or of intellectual changes following operation.

(Authors' Abstr.)

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Effects of Photic Stimulation During Sleep

The photic responses of five normal persons were investigated electroencephalographically during sleep. Photic responses were observed in all instances by means of automatic low frequency analysis. The responses tended to decrease with the deepening of sleep.

Next, the effect of light stimulation on 30 epileptic patients sensitive to light and 46 who were not sensitive to light was investigated during sleep. The sensitivity to light tended to be unchanged, reduced, or absent during sleep. The responsible factors seem to be the severity of the pathologic process and the effect of premedication necessary to induce sleep in some cases. Patients severely sensitive to light tended to remain light sensitive to the same degree in spontaneous sleep, while in medicated sleep a reduction or absence of these pathologic responses occurred. Patients mildly sensitive to light lost their light sensitivity even in spontaneous sleep. In no instance did sensitivity to light increase compared with that in the waking state. None of the 46 epileptic patients who were insensitive to light in the waking state became sensitive to it during sleep.

Seizure discharges in the electroencephalogram which produced clinical manifestations in the waking state became less effective in producing outward signs during sleep.

In two cases focal occipital sharp waves could be triggered by the flashing light during the waking state and during sleep.

The optic pathways to the cortex apparently remain patent during sleep although the threshold to stimuli rises. This rise in threshold may occur at the level of the lateral geniculate body.

(Authors' Abstr.)

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Study of Correlations between Electroencephalographic and Psychological Patterns in Emotionally Disturbed Children

1. The high percentage of abnormal EEG's in childhood schizophrenia (78·6 per cent.) suggests an organic basis or component in this particular condition. An EEG abnormality rate of 73·4 per cent. in the group of primary behavior disorders is in agreement with the findings of previous similar studies, and also suggests the probability of a defect or developmental retardation in the cerebral structure.

2. There is no apparent relationship between abnormality of the EEG and specific types of behavioral patterns such as extreme passivity, aggressiveness, or hyperactivity. Early head trauma and serious illness were also found with the same incidence among children of the emotionally disturbed group with normal EEG's as among the abnormal. Neither is there any apparent relationship between the EEG and specific emotional traits as suggested in the Rorschach test, with the possible exceptions of the apperceptive approach and form quality.

3. The greater the cerebral dysfunction, as indicated by the EEG, the more abnormal do we find specific psychological variables dealing with perception, perceptual-motor functions, and the body image.

4. Gross distortions in visual motor Gestalt functions, in body image, and in perceptual and motor functions in general appear related to foci and asymmetries in the EEG, most notably in the occipital areas.

5. The alpha percentage may be related to the accuracy of form perception as reflected by the Rorschach test. This accuracy of perceptual association appears to become impaired in the presence of foci in the EEG, especially occipital foci.

6. The results of the study tend to support Schilder's contention that organic damage to the brain causes a disturbance in perception and motility and therefore adversely affects the body image.

(Authors' Abstr.)

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An Experimental Study of the Etiology of "Rum Fits" and Delirium Tremens

1. Ten healthy morphine addicts who had been abstinent from narcotics for at least 3 months volunteered for a study of chronic intoxication with alcohol. The objective was to maintain each subject continually in the maximum state of intoxication compatible with safe

ambulatory management for a period of 6 to 13 weeks, and then to discontinue alcohol abruptly.

2. Alcohol was given orally at intervals of 1 or 2 hours from 6 a.m. to 12 midnight, with supplementary drinks at 2 a.m. or 3 a.m., and in an average daily dose of 266 to 489 ml. of 95 per cent. ethyl alcohol for 7 to 87 days.

3. Convulsions and delirium did not appear during the period in which patients were consuming large amounts of alcohol sufficient to maintain high blood alcohol levels.

4. Three patients withdrew from the experiment after 16 days of drinking, or less, and one after 34 days of drinking. The symptoms following discontinuance of alcohol by these patients were mild, consisting chiefly of tremulousness, nausea, perspiration and insomnia, and of brief duration.

5. Six of the patients drank for 48 to 87 days. Following abrupt withdrawal of alcohol, all developed tremors, marked weakness, nausea, vomiting, diarrhoea, hyperreflexia, fever and hypertension. Two of these six patients had seizures; three had a frank delirium (one of these was receiving large amounts of barbiturates at the time delirium occurred); two had transient visual or auditory hallucinations or both; and one escaped both convulsions and hallucinations. These phenomena occurred despite the ingestion of an adequate diet, with multiple vitamin supplements, throughout the periods of intoxication and withdrawal.

6. The intensity of symptoms following withdrawal of alcohol appeared to be correlated roughly with amount of alcohol consumed and with the length of the period of intoxication.

7. A characteristic electroencephalographic pattern was obtained during chronic intoxication with alcohol and during the withdrawal period. Early during chronic intoxication, the EEG's were generally slowed whenever the patients had high blood alcohol levels and were showing clinical evidence of intoxication. Later during chronic intoxication, the EEG's were not as slow, even though blood alcohol levels were higher than during the early part of the period of intoxication. Following withdrawal of alcohol, the EEG first became normal. Between the 16th and 33rd hours of abstinence, the percentage of alpha activity declined and random spikes and bursts of slow waves were observed.

8. The concentration of alcohol in the blood (usually determined with an automatic breathmeter) was followed in three of the patients. As long as the patients were drinking between 397 and 466 ml. of alcohol daily or less, blood alcohol levels were less than 50 mg. per 100 ml. and clinical evidence of intoxication was not present. Elevation of the alcohol intake to between 430 and 479 ml. per day was followed by a rise in blood alcohol levels to between 150 and 250 mg. per 100 ml., accompanied by evidence of marked intoxication. When the dosage of alcohol which initially caused high blood alcohol levels was maintained, the concentration of alcohol in the blood fell slowly and nearly reached zero. A small increase in the dosage of alcohol and a change in the schedule of drinking was followed by a second elevation in the blood alcohol concentrations. Thereafter blood alcohol levels did not fall until alcohol was withdrawn.

9. No evidence of residual impairment could be detected 3 months after discontinuance of drinking, as judged by physical, psychiatric, psychological, laboratory, and electroencephalographic examinations.

(Authors' Abstr.)

The "Craving" for Alcohol. Formulation of the Joint Expert Committees on Mental Health and on Alcohol

The terms craving, irresistible desire, need, and sometimes appetite, have been employed in the alcohol literature to explain certain or all forms of abnormal drinking behavior seen in alcoholics.

There exists a variety of alcoholic drinking behavior which specifically suggests "craving" in the vernacular sense, but closer analysis reveals that different mechanisms are at work and that a term such as "craving" with its everyday connotations should not be used in the scientific literature to describe them if confusion is to be avoided.

The onset of the excessive use of alcohol, the drinking pattern displayed within an acute drinking bout, relapse into a new drinking bout after days or weeks of abstinence, continuous daily excessive drinking and loss of control, are all behaviors which have been claimed to be manifestations of "craving" of the same order.

"Craving" and its alternative terms have been used to explain drinking arising from (*a*) a psychological need, (*b*) the physical need to relieve withdrawal symptoms, or (*c*) a physical need which originates in physiopathological conditions involving metabolism, endocrine functions, etc., and existing in the alcoholic before he starts on his drinking career or developing in the course of it.

It has been pointed out by some investigators that a physical craving for alcohol, as indicated by withdrawal symptoms, is seen immediately following withdrawal of alcohol only after prolonged, continuous and heavy use; such a physical craving cannot be postulated as the cause of the resumption of drinking after a considerable period of abstinence when withdrawal symptoms are no longer present.

The Joint Committees feel that a sharp distinction should be drawn between (*a*) the processes operative immediately after withdrawal of alcohol in the situation described above, and (*b*) those which lead to resumption of drinking after the disappearance of withdrawal symptoms.

Since, on the interruption of continuous drinking, the distressing withdrawal symptoms provoke the alcoholic to seek relief from them by the use of more alcohol, the Joint Committees would prefer to refer to this condition as a physical dependence on alcohol.

During a period of abstinence, even in the absence of withdrawal symptoms, one observes clinically the building up of psychological tension which provokes a pathological desire for alcohol as a means of relieving this tension; in this condition the individual may be said to be psychologically dependent on alcohol.

It must be pointed out, however, that mounting psychological tension is not the only cause of resumption of drinking. It can also be caused by social pressure to drink, or sometimes even by the accidental ingestion of alcohol.

In addition, a physiopathological condition (other than physical dependence) cannot be excluded as one of the factors which may lead to the resumption of drinking after days or weeks of abstinence.

In all alcoholics, regardless of whether they have an abnormal disposition or suffer from any acquired mental disorder, one observes a weakening of that part of the higher personality from which the inhibition of primitive tendencies derives. As a result, there appears a release of the primitive side of the personality. The pathological desire for alcohol therefore becomes more evident as the inhibiting forces weaken and ultimately fail.

There is also a relatively small group of drinkers in whom the pathological desire for alcohol appears practically at the beginning of their drinking career, instead of after many years, and can thus lead to a rapid development of alcoholism. Among these will be found certain types of psychopath (e.g. the volitionally weak and the impulsive personalities). It may occur also in certain cases of somatic or mental disorder (for instance, in post-concussion states, epilepsy, certain psychoses, and oligophrenia). There is, however, a minority in this group who show none of these conditions and yet manifest a pathological desire for alcohol from the beginning of their drinking history.

The Effects of Solid Food and of Alcoholic Beverages, especially Wine, on the Excretion of Hippuric Acid

The experiments described herein were carried out in healthy young subjects in order to study the effects of alcoholic beverages, especially wine, on the excretion of hippuric acid following the ingestion of sodium benzoate. The urinary excretion of hippuric acid was studied for a period varying from 6 to a maximum of 10 hours under the following experimental conditions: (1) on an empty stomach, (2) after a meal without wine, (3) after a meal with wine, (4) after an aqueous solution of ethyl alcohol on an empty stomach, and (5) after wine on an empty stomach.

1. The administration of the test dose of 6 g. of sodium benzoate after a meal caused a higher excretion of hippuric acid than that observed following its administration on an empty stomach.

2. Wine ingested on an empty stomach did not substantially affect the total amount of hippuric acid excreted following the administration of sodium benzoate but did delay and prolong its excretion.

3. Ethyl alcohol in aqueous solution definitely decreased the total amount of hippuric acid excreted after the administration of sodium benzoate, and also delayed and prolonged its excretion.

4. Wine with a meal caused a marked increase in the excretion of hippuric acid as well as an earlier and more prolonged period of hyperhippuricuria.

(Authors' Abstr.)

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Brief and popular review of the data on the metabolism in the brain and on the chemistry of transmission of a nerve stimulus.

M. Hoseh (Chem. Abstr.)

Physiological Factors Influencing Brain Glycogen of the Mouse. Chance, M. R. A., and Walker, A. P. (Univ. Birmingham, Engl.). [*J. Endocrinol.*, **10**, 316–24 (1954); *cf. C.A.* 45, 5317*d*].

Intravenously injected glucose increased brain glycogen concentration (I) of the mouse and caused a 40 mg. per cent. increase in blood glucose. Injection of the anti-insulin principle of the anterior pituitary also increased (I), as did adrenaline. Neither insulin, cortisone, deoxycorticosterone glucoside, nor fasting affected (I). During metrazole-induced convulsions, none of these substances influenced (I) significantly, except for insulin, which reduced (I) with the characteristic decrease in blood glucose. The changes in blood glucose with (I) with some types of activity are presented, and it is concluded that they represent independent responses resulting from central nervous activity.

KATHRYN KNOWLTON (Chem. Abstr.)

Microchemical Investigation of Oxalic Acid in Cerebrospinal Fluid. Berisso, Benjamin. [*Pubs. inst. invest. microquim., Univ. nacl. litoral* (*Rosario, Arg.*), **17**, 235–42 (1953).]

Various methods are studied for identifying oxalic acid in the cerebrospinal fluid, involving the formation of crystals. Such reagents as $Sr(NO_3)_2$, $CdSO_4$, and yohimbine-HCl are used, and the sensitivity of the reaction, interferences, and physical characteristics of the oxalate formed are reported.

R. B. BRADSTREET (Chem. Abstr.)

Metabolism of Nucleic Acids in the Liver and CNS. Chepinoga, O. P., Skvirskaya, E. B., Ruskina, L. P., and Siliech, T. P. (*Biochem. Inst. Acad. Sci. Ukr. S.S.R., Kiev*). [*Ukrain. Biokhim. Zhur.*, **24**, 177–85 (in Russian, 185–7), (1952); *cf. ibid.*, **23**, *No.* 3 (1951).]

Brain and liver nucleic acid metabolism was studied in 150-g. white rats as follows: (1) controls; (2) after partial liver excision; (3) during prolonged narcosis; (4) a combination of (2) and (3). The left lower portion of the liver (about one-third of the total liver wt.) was removed under ether. Sodium medinal (15 mg./100 g. wt., 3–4 times daily) was used for narcotic sleep induction. Determined were: total nucleic acid (NA) P, ribonucleic acid (RNA) P, deoxyribonucleic acid (DNA) P, ribonuclease (RNAase) and deoxyribonuclease (DNAase) in liver and brain tissues. With (2) a decrease in NA P resulted in both brain and liver, enzyme activity increasing except for DNAase in the liver where it decreased. In (3) the effect on the CNS led to lowered NA P in brain and liver, and decreased enzyme activity except for DNAase of the brain which increased. (4) Was not the summative effect of (2)+(3) since the new metabolic pattern from (2) is further changed by (3). A modified Schmidt-Tannhauser method (cf. Chepinoga, Skvinskaya and L. P. Rukina, *Ukrain. Biokhim. Zhur.*, **23**, No. 3 (1951)) was used for total NA P. DNAase was determined viscometrically. A RNAase determination was developed based upon the Kunitz method (C.A.34, 7944[4]) as follows: Determination A: 0·5 ml. of 0·1 M acetate buffer (pH 6·4), 0·5 ml. of 1-hr. 1:10 aqueous extract of minced tissue, and 1·0 ml. 0·4 per cent. Na salt of RNA. Determination B: 0·5 ml. of 0·1 M acetate buffer (pH 6·0), 0·5 ml. of extract, and 1·0 ml. H_2O. All samples were incubated 1 hr. at 37°, 2·0 ml. of 0·35 per cent. uranyl acetate with 5 per cent. CCl_3COOH added. left an additional 30 min. at 37° to precipitate proteins and remaining RNA, and then filtered. One ml. of filtrate was digested with 0·15 ml. of concentrated H_2SO_4 and P. determined colorimetrically, comparing both A and B against their respective controls.

CLAYTON F. HOLOWAY (Chem. Abstr.)

Exchange of Substances in the Brain During Excitation. Palladin, A. V. [*Zhur. Vysshei Nervnoi Deyatel. im. I.P. Pavlova*, **3**, 801–8 (1953).]

Rabbits were administered subcutaneously in a single dose pervitin, 5–8 mg./kg., or metrazole, 50–70 mg./kg., and beheaded 1, 2, or 4 hrs. after the injection. The brain was removed and frozen in liquid air. To prevent effects of beheading on labile P compounds, the rabbits were first instantly killed by intravenous injection of 1 ml. of 10 per cent. hexonal. Adenosinetriphosphate (A.T.P.) and inorganic P were determined. Injection of pervitin lowers ATP concentrations 1 hr. after injection, and raises the concentration of inorganic P. The values for both return to normal within 4 hrs. Metrazole raises ATP and lowers the inorganic P concentration 1 hr. after injection, the values becoming normal within 4 hrs. P^{32} was injected simultaneously with pervitin or metrazole, and relative specific activities of P^{32} of ATP and inorganic P in the brain were determined 1–4 hrs. after injection. With pervitin there was an increase in the ATP exchange; after metrazole, lowered exchange of ATP with no variation up to 4 hrs. No changes in the phospholipide content was noted after either pervitin or metrazole. By employing P^{32}, however, after pervitin administration the extent of incorporation of P^{32} into saturated phospholipides is greatly increased 1 hr. after the injection, returning to normal within 4 hrs. The incorporation of P^{32} into unsaturated phospholipides after pervitin is somewhat above normal, falling below normal within 4 hrs. Pervitin stimulates the central nervous system, thereby raising its working capacity, while metrazole stimulates the brain without raising its working capacity. Chronic overstimulation by means of daily application of electric current for 1–1·5 months to rats or by production of insomnia in rats for 3 days lowered the ATP of the brain. Glycogen content is unaltered in insomnia, but in overstimulation by electric current it is somewhat increased, accom-

panied by lowering of the activity of phosphorylase. During overstimulation by electric current in rats there is no change in the level in ribo- or deoxyribosenucleic acid in the brain, but the activity of deoxyribonuclease is lowered. By means of P^{32} it was shown that the exchange of the nucleic acids during overstimulation is reduced, suggesting lowered synthesis of proteins in the brain during overstimulation. These and previous data are inconsistent with the view that the level of deoxyribosenucleic acid in the cell nucleus is constant, and that it plays a role only during division. Changes in the activity of deoxyribonuclease correspond with the appearance of new functions, being connected with an increase in differentiation of organs and tissues.

J. A. Stekol (Chem. Abstr.)

Action of Diet on the Level of Pyruvic and Lactic Acids in Blood and Cerebrospinal Fluid in Mental Diseases. De Franciscis, P., and Lampitella, P. [*Boll. soc. ital. biol. sper.*, **29**, 260–3 (1953).]

The diet of psychiatric patients was found to be deficient in lipides, Ca, P and vitamins. These patients had, as was shown in a previous study, increased levels of pyruvic acid in blood (I) and cerebrospinal fluid (II). In (II) the lactic acid content was increased up to 50 per cent. After the diet of 10 patients was balanced to normal requirements for 3 months, determinations were made on (I) and (II) of pyruvic and lactic acids. It was found that: lactic acid in (I) and (II) was normal; pyruvic acid was less than in the patients with the deficient diet.

J.C.C. (Chem. Abstr.)

Total Lipide and Plasmalogen Contents of the Brain in Experimental Hyperthyroidism. Minder, W. H., and Abelin, I. (*Univ. Bern. Switz.*). [*Helv. Physiol. et Pharmacol. Acta*, **12**, 63–73 (1954 (in German).]

In rats with hyperthyroidism induced by feeding thyroid material for 10–28 days there was no change or perhaps a slight increase in total lipides of the brain. Another group fed a high-fat diet for 1– days showed no change in total brain lipides. No change in plasmalogen content was observed in either group.

L. E. Gilson (Chem. Abstr.)

Phosphocreatine and Adenosinetriphosphate (ATP) Changes in Brain Cortex after Electroconvulsions. Minaev, P. F., and Kurokhtima, T. P. (*Inst. Biol. and Med. Chem., Acad. Med. Sci. U.S.S.R., Moscow*). [*Ukrain. Biokhim. Zhur.*, **21**, 359–62 (1949) (in Russian).]

The content of phosphocreatine (I) and of ATP (II) decreases sharply after convulsions and before a second stimulus in effective, excitability of the cortical motor zone decreasing sharply at the same time; 30 min. after termination of convulsions, the contents of (I) and of (II) in the cortex return to normal, by which time excitability of the cortex has been considerably restored. Trephination of the dog skull was carried out under morphine-ether-chloroform or ether-chloroform; 30 min. after incision of the dura mater, excitability of the cortical motor zone was determined by a constant current from Ag electrodes of a chronaximeter, and was established by contraction of the hind paw extensor muscles. Having determined excitability, a portion of the cortex was excised from one control lobe by a surgical spoon chilled in liquid air and the sample frozen in liquid air, no more than 2–3 sec. lapsing from moment of sampling to immersion in liquid air. Five minutes after the excision, convulsions were produced by electric current, one electrode on the lower lip, the second on the neck muscles. Duration of the irritation was 2–3 sec., with 1-min. intervals between convulsions. It was not possible to obtain more than 5–12 seizures in a row, the last attacks being short and weak. Convulsions having ceased, a portion of cortex from the 2nd lobe was similarly extended, frozen, and the excitability determined every 5–10 mins.; 30 mins. after termination of convulsions, one more portion of cortex was excised and frozen. Each of the 3 portions of cortex were ground to a powder while frozen and cooled-8 per cent CCl_3COOH was added (1:10). The following P compounds were determined in the filtrate: (1) inorganic P, after precipitation with Mg. mixture, (2) some inorganic P+phosphocreatine P, (3) P after 10-min. hydrolysis in 1N HCl at 100°. P. was determined colorimetrically according to Fiske and SubbaRow in a step photometer.

Clayton F. Holoway (Chem. Abstr.)

Adenosinetriphosphate (ATP) and Phosphocreatine Changes in Brain Cortex after Corazole Convulsions. Levyant, M. I., Malkiman, I. I., and Kamenetskaya, B. I. (*Inst. Biol. and Med. Chem., Acad. Med. Sci. U.S.S.R., and Central Inst. Psychiat., Moscow*). [*Ukrain. Biokhim. Zhur.*, **21**, 363–7 (1949) (in Russian).]

There is a considerable decrease in ATP (I) and phosphocreatine (II), an increase of inorganic P, and excitability of the cerebral motor zone is sharply depressed; this is in accord with the hypothesis that ATP is an energy source of cortical excitation. Bilateral trephinations of dogs under morphine-ether narcosis were made, and the dura removed; 1·5–2 hrs. after operation, when the dog showed pupillary reflexes, 1–1·5 g. of cortex was excised and immediately immersed in liquid air. After 1 hr. 0·25 ml. of 10 per cent. corazole soln./kg. wt. was injected intravenously via a glass cannula in the femoral vein. Following

a latent period of 15–20 sec., tonic and then clonic convulsions of 2–3 min. duration set in, immediately after which a second symmetrical sample was excised. One hour after the second sample, a series of consecutive convulsions were induced, corazole being injected immediately after cessation of convulsions, and a third sample was taken. Rheobase for the normal motor zone was also determined. After single and multiple attacks, excitability was determined by a chronaximeter, the active electrode (a swab moistened in Ringer solution and connected by a thin Ag rod) being placed on the motor zone, the indifferent electrode (Ag tube) being placed in the rectum. Excitability was established by threshold contraction of the extensor muscles of the hind contralateral limb. Samples were analyzed for inorganic P, (I) and (II). Frozen samples were powdered and then ground in a porcelain mortar with 4 per cent. CCl_3COOH (1:4), protein precipitation, being limited to 10 min. to avoid rupture of labile P compounds (II). (I) was precipitated in 1 filtrate by additions of 25 per cent. mercuric acetate (0·25 ml./3 ml. of CCl_3COOH filtrate). To a second portion of filtrate (1 ml.) NaOH was added to a light phenolphthalein pink, followed by 0·2 ml. of 25 per cent. barium acetate. Inorganic P was determined in the precipitate and (II) in the centrifugate.

CLAYTON HOLOWAY (Chem. Abstr.)

Effect upon Depleted Nerve Centers of Adenosinetriphosphate (ATP) Introduced into the Brain Ventricles. Minaev, P. F. (Inst. Biol. and Med. Chem., Acad. Med. Sci. U.S.S.R., Moscow). [*Ukrain. Biokhim. Zhur.*, **21**, 368–73 (1949) (in Russian).]

Injection of ATP into the ventricles changes the composition of nerve centers depleted by epileptic seizures, enabling them to regain activity toward electrical stimulation. After exclusion of brain glycolysis by monoiodoacetate inactivation, and after failure of the animal to react to electrical stimulation by manifesting epileptic convulsions, the introduction of ATP into the brain ventricles makes it possible for convulsions to begin anew.

CLAYTON F. HOLOWAY (Chem. Abstr.)

Glycogen in the Brain Cortex under Normal and Pathologic Conditions. Shabadash, A. L. [*Ukrain. Biohkim. Zhur.*, **23**, 360–3 (1951) (in Russian).]

A didactic comparative discussion of microscopic and biochemical data previously recommended given by S. and others.

B. S. LEVINE (Chem. Abstr.)

Tweens as Substrates for Determination of the Lipase Activity of Brain. Bozzetti, E. [*Boll. soc. ital. biol. sper.*, **28**, 1087–9 (1952).]

Tweens 20, 40, 60, and 80, of the Atlas Powder Co., proved to be good substrates for quantitative determination of the lipase activity of brain tissues. The values obtained are lower than those obtained with tributyrin as substrates; tributyrin is considered not to be a substrate for lipase.

B.A. (Chem. Abstr.)

Phosphatase and Lipase Activity of the Brain. Bozzetti, E. [*Boll. soc. ital. biol. sper.*, **28**, 1089–90 (1952).]

Stress is laid upon the importance of stipulating the incubation time when carrying out a quantitative determination of phosphatase activity in the brain. Oscillations in values were paralleled by similar changes in lipase activity as found when using Tweens as substrate. There was direct proportionality between variations in the values obtained for alkaline phosphatase and those for lipase when acting upon polyoxyethylene sorbitan monolaurate (Tween 20). Such variations were not found with Tween 80 (polyoxyethylene sorbitan trioleate) and olive oil.

B.A. (Chem. Abstr.)

Brain Phosphorylases During Insulin Intoxication. Khaikina, B. I., and Goncharova, K. O. (Inst. Biochem. Acad. Sci. Ukr. S.S.R., Kiev). [*Ukrain. Biohkim. Zhur.*, **22**, 92–8 (99–100, in Russian) (1950); *cf. C.A.* 48, 6535a.]

The addition of insulin to enzymic brain preparations *in vitro* increases phosphorylase activity toward polysaccharide synthesis, but does not affect phosphatase activity. The introduction of large insulin doses during convulsions affects phosphatase and phosphorylase activities as follows: (1) phosphatase action is blocked; (2) phosphorylase activity in favour of synthesis remains at high level; at the same time, however, the polysaccharide synthesis mechanism decreases, e.g., at pH 6·2 polysaccharide synthesis is low in the absence of a seeder; (3) phosphorylase activity in favour of breakdown is somewhat increased.

CLAYTON F. HOLOWAY (Chem. Abstr.)

Factors Affecting Rat-brain Phosphatase Activity in Fresh Tissue Suspensions and in Histochemical Methods. Pratt, O. E. (Maudsley Hosp., London). [*Biochim. et Biophys. Acta*, **14**, 380–9 (1954) (in English); *cf. C.A.* 47, 12455h.]

A study was conducted to determine the effects of Pb^{++}, Ca^{++}, Mg^{++} and of the procedure for tissue preparation on the activity of acid phosphatase, alkaline phosphatase (I), adenosine-5′-phosphatase, adenosinetriphosphatase (II) and thiamine pyrophosphatase in rat-brain suspensions and in histochemical enzyme localization methods. Ca^{++} activates (I). Pb^{++}

generally inhibits the other enzymes in the histochemical system, but if its concentration is too low inorganic phosphate can be lost from the tissue, resulting in artefacts. Ca^{++} and Mg^{++} influence enzyme activity in the histochemical system in much the same way as they do in fresh tissue suspensions, except that (II) activation by Mg^{++} is reduced greatly by Pb^{++} present in the histochemical system.

MORTON PADER (Chem. Abstr.)

Metabolism of Glutamic Acid-1-C^{14} and Aspartic Acid-4-C^{14} in Rat Brain and Kidney Homogenates. Rayford, Claudia Ratcliff and Friedberg, Felix (Catholic Univ. of Amer., Washington, D.C.). [*Biochem. et Biophys. Acta*, **14,** 390–6 (1954) (in English).]

Whole rat kidney and brain homogenates utilize only the L-form of aspartic acid (I) and glutamic acid (II). Brain homogenate supernatant, however, may utilize a small amount of D-isomer. Whole rabbit kidney homogenate dissimilates D-I. Adenosinemonophosphate (AMP) and adenosinetriphosphate (ATP) inhibit (I) oxidation by kidney homogenate, but AMP stimulates it in brain. Diphosphopyridine nucleotide (DPN), triphosphopyridine nucleotide (TPN), pyruvate, and α-ketoglutarate increase dissimilation of (I) by both kidney and brain homogenates. AMP, ATP, DPN, TPN and oxalacetate stimulate (II) catabolism by rat kidney and brain homogenates. (I) and (II) oxidation by various tissues decreases in the order; liver, kidney, brain, spleen. Blood has no oxidizing activity. Oxidation rate is low in foetal liver, livers of Walker tumorbearing hosts, and in tumor tissue itself.

MORTON PADER (Chem. Abstr.)

The Relation Between the Oxidation of Glutamic Acid and the Synthesis of Acetylcholine in Brain Extracts. Kometiani, P. A. (Inst. Physiol. Acad. Sci. Georgian, S.S.R., Tiflis). [*Soobshecheniya Akad. Nauk Gruzin. S.S.R.*, **12,** *No.* 9, 531–8 (1951) (in Russian).]

In homogenates of rat brain the synthesis of acetylcholine (I) and phosphorylcholine (II) was slightly greater under aerobic than anaerobic conditions. With acetone powder extract of rat brain anaerobic conditions gave a great synthesis of (I). When ATP (adenosinetriphosphate), (II), and choline were all present in the reaction medium the highest synthesis of (I) was achieved. Omission of choline reduced the synthesis of (I) approximated 50 per cent. while omission of ATP lowered it by 95 per cent. When acetone powder extract was used, maximum synthesis of (I) was obtained on addition of diphospho-pyridine nucleotide, diaphorase, cytochrome oxidase, and cytochrome c. Niacinamide did not affect the synthetic rate. It was concluded that (II) plays an important role in the synthesis of (I) in brain tissue and *in vivo* the supply of (II) is maintained by formation of ATP with glutamic acid furnishing the energy source *via* oxaloacetate and the citric acid cycle.

JAY L. ROTH (Chem. Abstr.)

Ammonia-formation Systems in Brain Tissue. Tsukada, Yasuzo and Takagaki, Genkichiro (Keio Univ., Tokyo). [*Nature*, **173,** 1138–9 (1954).]

A homogenate prepared from instant-frozen guinea pig brain was incubated without substrate at 37°. After 10 min., a considerable amount of NH_3 was formed, glutamic acid as the source. Incubation for 30 min. showed that glutamine functioned as an NH_3-binding system rather than an NH_3-forming system. The NH_3 sources at this second stage were both glutamic acid and adenylic compound. After 50–90 min. incubation, NH_3 formation continued and glutamine decreased slowly. In this last period glutamine deamination was more active than glutamine synthesis.

J. D. TAYLOR (Chem. Abstr.)

The Localization of Abscesses in Brain with Radioactive Iodine. Burian, K., and Hoffmann-Credner, D. (2. Universitatsklinik, Vienna). [*Wien. Z. Nervenehilk. u. Grenzgebiete*, 306–14 (1953).]

Experiments with cats with artificially produced abscesses in brain *in vivo* showed that delivered I^{131} is stored in the abscesses and therefore may be located with sufficiently improved Geiger-Müller counters.

H.R.L. (Chem. Abstr.)

Encephalography in Vitamin B_1 Deficiency and Thiamine Shock. Mouriquand, G., Courjon, Jean, Edel, V., and Bonnet, H. [*Bull. acad. natl. med. (Paris)*, **136,** 580–5 (1952).]

Deficiency was produced in pigeons. Shock conditions developed after rapid intramuscular injection of 100 mg. thiamine in normal and deficient birds. In deficiency the changes in vestibular chronaxie precede by several days the appearance of electroencephalic changes. In thiamine shock, both effects coincide initially, but the electroencephalogram is delayed in its return to normal values as compared with the chronaxie. The disturbances caused by the shock are more clearly evidenced in the electroencephalogram.

A. E. MEYER (Chem. Abstr.)

Effect of Acetylcholine on the Electrical Activity of Peripheral Nerve. Legouix, Jean Paul and Minz, Bruno. [*Compt. rend.*, **238,** 1609–11 (1954).]

When the sciatic nerve of the pithed perfused frog was stimulated, the electrical activity of the peripheral branch of the nerve was recorded with the aid of an oscillograph. The

electrical activity was greatly enhanced and the amplitude of the maximum action potential was decreased if the perfusing Ringer solution contained equal parts of eserine and acetylcholine at 10^{-9} concentration.

W. Donald Graham (Chem. Abstr.)

Wallerian Degeneration in the Rat. The Effect of Age on the Concentration of Nucleic Acid and Phospholipide in Intact and Sectioned Nerves. Mannell, W. A., and Rossiter, R. J. (Univ. Western Ontario, London, Ca.). [*J. Exptl. Biol.*, **31**, 198–207 (1954).]

The concentrations of nucleic acid and phospholipide were correlated negatively with the weight of the sciatic nerve. After nerve section there was an increase in the concentration of nucleic acid and a decrease in the concentration of phospholipide. These changes took place more rapidly in smaller nerves from younger animals.

L.P.T. (Chem. Abstr.)

Content of Glycogen and Fermentable Sugar in the Brain During Abolition and Restoration of Life in the Organism. Gaevskaya, M. S. [*Zhur. Vysshei Nervnoi Deyatel. im. I.P. Pavlova*, **3**, 617–25 (1953).]

The brain of dogs, under ether, was exposed, and the animals were killed by bleeding from the hip artery. After 6 min. (time of clinical death) the animals were revived by blood transfusion and artificial respiration. No glucose was added to the transfused blood; adrenaline was added in the concentration of 1:1,000. Before bleeding, all dogs received heparin intravenously. The brain tissue was removed and frozen in liquid N_2, ground, and divided into two portions. One was analyzed for glycogen, the other for fermentable sugar and lactic acid. These were determined in the blood also. The glycogen content of the brain of the dying dog began to decrease in the first 3 mins. of "clinical death", reaching 10–30 mg. per cent. in the 5–6th min. During revival, the glycogen content of the brain did not reach normal levels until the lactic acid content of the brain became normal. Three to 6 hrs. after revival, when the sugar and lactic acid levels in the brain reached normal values, the glycogen content of the brain increased, returning to normal levels on the 3rd day. In the sixth minute of clinical death the brain retains some ability to ferment sugar. The quantity of nonfermentable sugar in the brain is independent of total reducing substances and of the state of the animal during death or revival.

J. A. Stekol (Chem. Abstr.)

Laboratory Reports on Gargoylism. Sartori, Ernesto (*Univ. Padova, Italy*). [*Atti soc. med.-chir. Padova*, **30**, 265–7 (1953).]

In 2 cases of gargoylism, serum mucoproteins calculated as tyrosine were 5·50 and 5·35 mg. per cent. compared with $3{\cdot}38 \pm 0{\cdot}27$ for normal adults and 2·50 to 3·50 for control babies of the same age. There was also a greater elimination of 11-oxycorticosteroids, i.e. 1·40, 1·35, 1·25 mg./24 hrs. compared with controls 0·30, 0·60 mg.

M.E. (Chem. Abstr.)

2. Pharmacology and Treatment.

Effect of Tetraethylthiuram Disulfide (*Antabuse*) *on the Alcohol Metabolism in vivo. Nowinski, Wiktor W., and Ewing, Paul L.* (*Univ. of Texas Med. Branch, Galveston*). [*Texas Repts. Biol. Med.*, **11**, 597–601 (1953).]

In pigeons fed Antabuse for several days and then given a single injection of EtOH, AcH accumulates in the blood in amounts comparable to those obtained in man. Since pigeon liver is devoid of xanthine oxidase, the effect of Antabuse cannot be based on inhibition of this enzyme, but must affect other enzymes concerned with the breakdown of AcH.

F.B.M. (Chem. Abstr.)

Convulsant Action of P-aminosalicylic Acid. Scarinci, V. (*Univ. Bologna*). [*Arch. sci. biol.* (*Italy*), **36**, 394–404 (1952).]

P-Aminosalicylic acid (I) applied directly to various regions of the nervous system in the toad (*Bufo viridis*), the frog (*Rana exculenta*), the pigeon, the rabbit, and the dog produced an epileptic state or hyperexcitability followed in some cases by a flaccid paralysis. These effects were not caused by the osmotic pressure of the solutions applied since solutions of NaCl and of Na salicylate at the same concentration produced no effect. The pronounced action on the nervous system appeared to be associated with the molecular configuration of the molecule. An NH_2 group para to the carboxylic group seems to be the structure responsible for the neurotropic properties of (I). Reactions to (I) depended both on the species and on the region applied. Local application to the dorsal surface of the spinal cord of the toad produced in order, increase in reflex excitability, tetanus, and finally flaccid paralysis. In both the frog and the toad (I) applied locally to the bulb caused paralysis. In dogs application of (I) to various regions of the brain caused clonus in the muscles under control of that region. Application to the zygomatic-temporal region decreased chronaxy in the area controlled by this region. Dogs made susceptible by pharmacological means to reflex epilepsy were easily put into an epileptic state by (I). In thalamic pigeons application of (I) to the optic lobes followed by the stimulation of reflexogenic cutaneous areas produced an epileptic state.

Epilepsy could not be induced after the lobes were removed. Application of (I) to the area of the cerebral cortex controlling the mouth region of the rabbit produced epileptiform electrical responses measurable by electrical recordings. Epileptic reflexes of the Jacksonian type were also produced in the mouth region without any reflex cutaneous stimulation. In general, the action of (I) was similar to that of strychnine.

NELLIE M. PAYEN (Chem. Abstr.)

Induction of Cortical Convulsion Current Centers by Narcotic and Hypnotic Agents and the Relation of the Focal Activity to the Convulsion Excitability of the Brain Cortex. Caspers, Heinz (Univ. Munster. Westfalen, Ger.). [*Z. ges. exptl. Med.*, **122**, 142–66 (1953).]

The effect of Et_2O, luminal, and evipan was studied electroencephalographically in rats. The drugs induced latent convulsion centers. The focal activity was related to the cortex excitability.

JOHN H. WEISBURGER (Chem. Abstr.)

Action of Nicotine and of Central Ganglioplegics on the Electrical Activity of the Brain. Longo, V. G., Berger, G. P. v., and Bovet, D. (Ist. super. sanita, Rome). [*J. Pharmacol. Exptl. Therap.*, **111**, 349–59 (1954).]

The effects of nicotine, Parpanit, Parsidol, Largactil, and Artane on the electroencephalogram of the rabbit are described.

L. E. GIBSON (Chem. Abstr.)

The Physiological Changes in Rabbit Induced by Electro-shock and the Influence of Several Drugs Thereupon. Kan, Noboru (Totori Univ. School Med.). [*Folia Pharmacol. Japan*, **48**, 42–51 (1952); *Breviaria*, 3–4 (in English).]

In rabbit 5 v. a.c. for 30 sec. did not cause an effect, 10 v. for 1 sec. gave varied results, and 15 v. for 1 sec. gave typical convulsion by electroshock; with d.c. the minimum effective amount was 40 v. for 1 sec. Repeated treatment produced resistance in rabbit against electroshock. Previous anesthesia with ether, urethan, and evipan Na produced some resistance against electroshock and mitigated the convulsion induced; morphine increased the degree of convulsion. $NaHCO_3$ sensitized the rabbit to electroshock and caused a stronger convulsion. Atropine, adrenaline, and pilocarpine slightly influenced the convulsion induced by the electroshock. The electroshock immediately influenced slightly, then decreased the leucocyte number, and the original level returned in 2 hours. The lymphocytes increased immediately, decreased, and then increased; pseudoeosinophil cells showed a reverse process to the lymphocytes. The blood pigment increased immediately, decreased, and finally increased to above the original level. Previous administration of drugs slightly influenced these effects, and those intensifying the convulsion increased the leucocyte number for a time. Respiration of rabbit was halted for 25 seconds after the electroshock and recovered with considerable agitation; the above drugs showed slight influence on this effect. The blood pressure increased with the convulsion by electroshock, gradually decreased, and then increased to normal; during the convulsion the cardiac movement was temporarily halted or decreased in activity. Compressing the abdominal aorta or removing intestine, spleen, and pancreas made the change in the blood pressure small, and removing the adrenal gland or administration of ergotamine did not allow the blood pressure to increase to the original level. Anesthesia by ether, $CHCl_3$ urethan, evipan Na, and alcohol decreased the blood pressure increase by the electroshock and morphine and $NaHCO_3$ intensified the increase. Administration of exciting agents caused temporary decrease of the blood pressure just after the electroshock. When the convulsion by the electroshock was eliminated by curare, the increase of blood pressure almost disappeared, indicating that the increase at the convulsion stage is due to the increase of resistance of the blood vessels by convulsion; contraction of blood vessels of central nervous nature may also participate in it. It was suggested that the blood-pressure decrease following the above increase is due to decrease of blood-vessel resistance due to muscular slackening together with the blood-vessel dilation of central nervous nature; participation of suppression of cardiac movement and acetylcholine formation was also suggested. The final increase of the blood pressure is chiefly due to adrenaline secretion by adrenal gland and sometimes to central excitement. The intestinal movement was temporarily inhibited by the electroshock; this was due to adrenaline secretion since previous removing of the adrenal gland or administration of ergotamine did not produce this effect. Inhibition of the intestinal movement by anesthetizing agents is eliminated by the electroshock in some cases. In parellel to the convulsion the brain wave was agitated by the electroshock. The changes induced by the electroshock in rabbit may be partially caused by the convulsion and partially by the excitement in the autonomic nerve center. Curare affected the former and ergotamine the latter; anesthetizing and exciting agents influence both. It was indicated that the effect of the electroshock is so great that small amounts of drugs did not much influence it.

SHOZABURO KITAOKA (Chem. Abstr.)

Tissue Distribution of a New Central Convulsant, 10–(2–dimethylaminopropyl)–9–acridanone. Mayer, S. E., and Bain, J. A. (Univ. of Illinois Med. Coll., Chicago). [*J. Pharmacol. Exptl. Therap.*, **111,** 210–23 (1954).]

The compound is a potent convulsant agent. In the symptoms it produces it resembles pentamethylenetetrazole. A sensitive specific method based on fluorescence is described for determination of its concentration in tissues. Intravenous injection of threshold doses in rats and cats results in marked concentration of the drug in brain and kidney. The concentration in the cerebral cortex is approximately 17$_{\gamma}$/g. of tissue when seizures are produced. Examination of the distribution in the central nervous system showed a correlation between the numbers of cell bodies in a given portion of the neuraxis and the amount of uptake of the drug.

L. E. Gilson (Chem. Abstr.)

The Effect of Central-nervous-system-stimulating Pharmacological Substances on the Absorption of Radioactive Iodine and on the Synthesis of Thyroxine of the Thyroid Gland. Kolli, E. A. (All-Union Inst. Exptl. Endocrinol., Moscow). [*Biokhimiya,* **19,** 273–9 (1954).]

Caffeine doses (5–128 mg.) and phenamine doses (0·03 mg.) augmented the absorption of radio-I by the thyroid gland. The effect becomes apparent on the third day and lasts for 8–10 days after drug administration. Beyond this period a reduction in absorption of the radio-I is accompanied by an increase in the weight of the thyroid gland and in the amount of organically bound I, causing an augmentation in the process of hormone generation and a consequent increase in the accumulation of thyroxine in the thyroid gland. High doses of caffeine and of phenamine are less effective than moderate doses.

B. S. Levine (Chem. Abstr.)

Action of Caffeine on the Spinal Reflexes in the Curarized and Decerebrate Frog. Gualtierotti, Torquato (Univ. Milan). [*Atti accad. nazl. Lincei, Rend., Classe sci. fis., mat. e nat.*, **16,** 384–6 (1954).]

The main effect of caffeine on the central nervous system consists in facilitating the convergence of sensory and motor impulses by decreasing the synaptic delay and producing a synchronized bombardment of the neurons. This produces a more accentuated basal depolarization of the medulla and an increasing synchronization of the synaptic potentials characterized by the appearance of a wave of larger amplitude and shorter duration, and caffeine and strychnine action is discussed.

A.E.M. (Chem. Abstr.)

The Activity of Some Central Depressant Drugs in Acute Decorticate and Diencephalic Preparations. Dasgupta, S. R., Mukherjee, K. L., and Werner, G. (School Trop. Med., Calcutta). [*Arch. intern. pharmacodynamie,* **97,** 149–56 (1954).]

Decorticate and diencephalic cats are much more sensitive to the depressant effects of R.P. 4560 and Pentothal than are normal cats. The effect of R.P. 4560 is especially enhanced. Transection of the base of the frontal lobes in front of the optic chiasma causes similar behavior changes as a decortication but the hypersensitivity to drugs is absent.

M. L. C. Bernheim (Chem. Abstr.)

Some Pharmacodynamic Properties of Chlorpromazine. Reuse, J. J. (Univ. Brussels, Belg.). [*Compt. rend. soc. biol.*, **148,** 192–3 (1954).]

The adrenolytic, ganglioplegic, and antihistaminic actions of chlorpromazine are described.

L. E. Gilson (Chem. Abstr.)

The Interaction of Barbiturates With Serum Albumin and Its Possible Relation to Their Disposition and Pharmacological Actions. Goldbaum, Leo R., and Smith, Paul K. (George Washington Univ., Washington, D.C.). [*J. Pharmacol. Exptl. Therap.*, **111,** 197–209 (1954).]

Ultrafiltration studies show that the reversible binding to bovine albumin of numerous common barbiturates is related to the length and nature of the side chains. Binding is related to pH and is maximal at pH 7·8–8·0. With increasing drug concentration the fraction bound decreases but the total amount bound increases. With increasing protein concentration the fraction of drug bound approaches a maximum. Thiopental is more strongly bound than comparable barbiturates and will partially displace them from serum albumin. It in turn can be displaced by Na lauryl sulfate. Rabbit tissue homogenates can bind larger fractions of barbiturates than can be accounted for by their serum albumin content. The extent of bindings *in vitro* seems related in part to the distribution of the drugs *in vivo*. The extent of protein binding correlates fairly well with the known pharmacological properties of the drugs.

L.E.G. (Chem. Abstr.)

The Effect of Caffeine on Activity of the Higher Nervous System in Mice. I. Use of Various Single Doses of Caffeine. Vikt. K. Fedorov. [*Zhur. Vysshei Nervnoi Deyatel. im. I.P. Pavlova,* **3,** 626–35 (1953).]

Caffeine in doses of 0·01–0·07 mg. per mouse increases responses to conditioned reflexes with no after-effects of caffeine on the animal. Doses of 0·1–0·7 mg. per mouse produce a

sharp initial response, followed by a depressing effect: 2–3 days later the responses return to normal. Doses of 1–5 mg. per mouse produce effects similar to those of medium doses, but more sharply defined, which last for up to 10 days. Chronic administration of medium and large doses of caffeine for up to 2–4 months lowers significantly conditioned reflex activity in mice, owing in part to the effects of all the procedure of administration of caffeine to mice. In all cases caffeine was fed to mice with small amounts of food, which was consumed in 2–3 minutes.

J. A. Stekol (Chem. Abstr.)

Effects of Adenosinetriphosphate on Electrical Activity of the Brain During Preconvulsive and Convulsive Phases Induced by Various Convulsants. Torda, Clara (*Cornell Univ. Med. Coll., New York, N.Y.*). [*Am. J. Physiol.*, **178**, 123–8 (1954); *cf. C.A.* **47**, 7677a).]

Adenosinetriphosphate (ATP) induced a temporary inhibition of the changes of the cerebral activity caused by physostigmine salicylate during both the preconvulsive and convulsive phases. Physostigmine apparently acts mainly through an increase of the acetylcholine content of the brain. ATP inhibited some of the changes induced by pentylenetetrazole (I) and did not modify others. (I) induces convulsions by the interaction of at least 2 mechanisms; an increase of the acetylcholine content of the brain and another, not yet identified, process. It is suggested that the spiking and increase of the voltage of the brain waves induced by acetylcholine are interrelated with a metabolite appearing during the resynthesis of ATP. One of the mechanisms through which a dynamic equilibrium between the content of ATP and acetylcholine in the brain is maintained was described. This regulation results from the property of ATP to increase acetylcholine synthesis and the property of acetylcholine to increase splitting of ATP by adenosinetriphosphatase.

E. D. Walter (Chem. Abstr.)

Narcotics and Brain Respiration. Ghosh, J. J., and Quastel, J. H. (*Montreal Gen. Hosp., Can.*). [*Nature*, **174**, 28–31 (1954).]

The increased respiration of rat brain cortex *in vitro*, brought about by K ions or 2,4-dinitrophenol (I), is suppressed or eliminated by the presence of pharmacologically active concentrations of phenobarbital, thiopental, and chloretone. The increased sensitivity of the respiration of stimulated brain cortex to narcotics is due to a retarding effect of the narcotics on a specific phase of nerve respiration that is K-sensitive and concerned with glucose (or pyruvate) oxidation. This phase is not prominent in a resting, unstimulated nerve, the respiration of which is made up largely of processes that are unresponsive to K or insensitive to low concentrations of narcotics. This phase, however, becomes an important aspect of the respiration of stimulated nerve. The presence of EtOH at 0·1 per cent. brings about 20 per cent. inhibition of the respiration of rat brain cortex stimulated by K or (I). The same concentration of EtOH increases the respiration of unstimulated brain cortex, probably by undergoing an oxidation, which is obscured by the stimulation of respiration in a glucose medium by the addition of K ions or (I).

J.D.T. (Chem. Abstr.)

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(R.) indicates a *Review*; the title of the book reviewed is followed by the author's name.

(E.) indicates the *Epitome* section; the title of the epitome is followed by the author's name.

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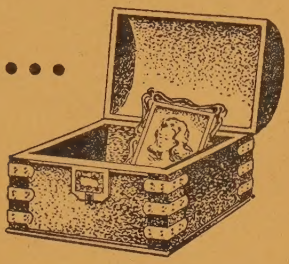

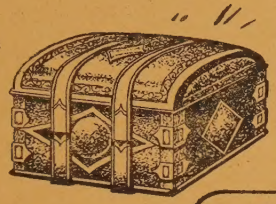

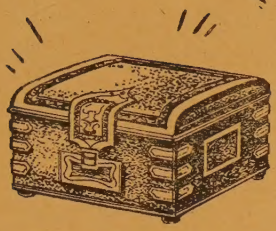

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